UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**
OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2025
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission file number: 001-40530

GH Research PLC

(Exact name of Registrant as specified in its charter)

Ireland
(Jurisdiction of incorporation or organization)

Joshua Dawson House
Dawson Street
Dublin 2
D02 RY95
Ireland
(Address of principal executive offices)

Velichka Valcheva, MD, MSc
Chief Executive Officer
Joshua Dawson House
Dawson Street
Dublin 2
D02 RY95
Ireland
+353 1 437 8334
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Copies to:

Deanna L. Kirkpatrick
Yasin Keshvargar
Davis Polk & Wardwell LLP
450 Lexington Avenue
New York, NY 10017
(212) 450-4000

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Ordinary shares, nominal value $0.025 per share	GHRS	The Nasdaq Stock Market LLC

Securities registered or to be registered pursuant to Section 12(g) of the Act:
None

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:
None

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report.

Title of Class	Number of Shares Outstanding
Ordinary shares	62,029,395

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes ☐ No ☒

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter during the preceding 12 months (or for such shorter period that the registrant was required to submit such files):

Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or an emerging growth company. See definition of "large accelerated filer", "accelerated filer", and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large Accelerated Filer ☐	Accelerated Filer ☒	Non-accelerated Filer ☐ Emerging Growth Company ☒

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards † provided pursuant to Section 13(a) of the Exchange Act. ☐

† The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

☐ U.S. GAAP

☒ International Financial Reporting Standards as issued by the International Accounting Standards Board

☐ Other

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.

☐ Item 17 ☐ Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes ☐ No ☒

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PRESENTATION OF FINANCIAL AND OTHER INFORMATION

Unless otherwise indicated or the context otherwise requires, all references in this Annual Report to the terms "the Company," "we", "us" and "our" refer to (i) GH Research Ireland Limited prior to the completion of our corporate reorganization in connection with our initial public offering, or the Corporate Reorganization, and (ii) GH Research PLC (and, where the context requires, its subsidiary) following the completion of the Corporate Reorganization. For information on our Corporate Reorganization, see Exhibit 2.1 to this Annual Report.

Financial Statements

Our financial information is presented in U.S. dollars. We prepare our consolidated financial statements in accordance with the IFRS Accounting Standards as adopted by the International Accounting Standards Board (IASB). The terms "dollar," "USD" or "$" refer to U.S. dollars and all references to "€" are to euro.

Market and Industry Data

This Annual Report contains industry, market and competitive position data that are based on general and industry publications, surveys and studies conducted by third parties, some of which may not be publicly available, and our own internal estimates and research. Third-party publications, surveys and studies generally state that they have obtained information from sources believed to be reliable, but do not guarantee the accuracy and completeness of such information. These data involve a number of assumptions and limitations and contain projections and estimates of the future performance of the industries in which we operate that are subject to a high degree of uncertainty. We caution you not to give undue weight to such projections, assumptions or estimates.

Rounding

We have made rounding adjustments to some of the figures included in this Annual Report. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains statements that are, or may be deemed to be, forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Section 27A of the Securities Act of 1933, as amended, or the Securities Act. All statements other than statements of historical fact included in this Annual Report, including statements regarding our plans and expectations with respect to progressing development of GH002; our targets regarding the initiation of our first global pivotal program; our business strategy, product candidates, medical devices required to deliver these product candidates, ongoing and currently planned nonclinical studies and clinical trials, regulatory submissions and approvals and their effects on our business strategy, our expectations related to commencing trials in the United States, research and development costs, cash runway, as well as plans and objectives of management for future operations, are forward-looking statements. Many of the forward-looking statements contained in this Annual Report can be identified by the use of forward-looking words such as "may", "anticipate," "believe," "could," "expect," "should," "plan," "intend," "estimate," "will", "potential" and "ongoing," among others.

Forward-looking statements appear in a number of places in this Annual Report and include, but are not limited to, statements regarding our intent, belief or current expectations. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified under "Item 3. Key Information—D. Risk Factors." These risks and uncertainties include, among others, factors relating to:

- the commencement, timing, progress and results of our research and development programs, nonclinical studies and clinical trials;

- the timing, progress and results of developing and conducting clinical trials for our GH001 and GH002 product candidates and the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001, for our initial and any additional indications;
- our efforts to expand into other jurisdictions such as the United States and in Europe;
- our expectations related to the technical development and expansion of our external manufacturing capabilities for our GH001 and GH002 product candidates as well as the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001;
- our reliance on the success of our GH001 and GH002 product candidates;
- the timing, scope or likelihood of regulatory filings and approvals by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other comparable foreign regulatory authorities, for our GH001 and GH002 product candidates and our initial and any additional indications;
- our expectations regarding the size of the eligible patient populations for our GH001 and GH002 product candidates, if approved for commercial use;
- our ability to identify third-party clinical trial sites to conduct trials and our ability to identify and train appropriately qualified therapists to administer our investigational therapy;
- the effect of pandemics, such as the COVID-19 pandemic, epidemics, outbreaks of an infectious disease or similar events on aspects of our business or operations, including delays in the regulatory approval process, contracting with clinical trial sites and engaging in clinical trials;
- our ability to implement our business model and our strategic plans for our business and GH001 and GH002 product candidates;
- our ability to identify, develop or acquire and obtain approval by the FDA, EMA or other comparable foreign regulatory authorities of medical devices required to deliver our GH001 and GH002 product candidates, such as our proprietary aerosol delivery device for GH001;
- our commercialization and marketing capabilities and strategy;
- the effects of undesirable clinical trial outcomes and potential adverse public perception regarding the use of mebufotenin and psychedelics generally on the regulatory approval process and future development of our product;
- the pricing, coverage and reimbursement of our GH001 and GH002 product candidates, if approved;
- the scalability and commercial viability of our manufacturing methods and processes;
- the rate and degree of market acceptance and clinical utility of our GH001 and GH002 product candidates;
- our reliance on third-party suppliers for our nonclinical study and clinical trial drug substance and product candidate supplies, as well as key raw materials used in our manufacturing processes;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;
- our expectations regarding potential benefits of our GH001 and GH002 product candidates and our approach generally;
- our expectations around regulatory development paths and with respect to the federal Controlled Substances Act, or CSA, classification;

- the scope of protection we and any current or future licensors or collaboration partners are able to establish and maintain for intellectual property rights covering our GH001 and GH002 product candidates;
- our ability to operate our business without infringing, misappropriating, or otherwise violating the intellectual property rights and proprietary technology of third parties;
- our ability to protect our intellectual property rights, including enforcing and defending intellectual property-related claims;
- regulatory developments in the United States, under the laws and regulations of the European Union, or EU, and other jurisdictions;
- continuing inflation, imposition of tariffs and trade barriers, interest rates and foreign currency exchange rates, disruptions in global supply chains and labor markets, and geopolitical risks and global hostilities, including any direct or indirect economic impacts resulting from conflict in Eastern Europe and the Middle East and the political, economic and social instability in Venezuela, tariff and trade wars, or increased tensions between China and Taiwan;
- developments and projections relating to our competitors and our industry;
- our ability to maintain an effective system of internal control over financial reporting;
- the amount of time that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations and capital expenditures;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- our ability to effectively manage our anticipated growth;
- our ability to attract and retain qualified employees and key personnel;
- whether we are classified as a passive foreign investment company for current and future periods;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart our Business Startups Act of 2012, or the JOBS Act, and a foreign private issuer;
- the future trading price of the ordinary shares and impact of securities analysts' reports on this price; and
- other risks and uncertainties, including those listed under "Item 3. Key Information—D. Risk Factors."

These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions described under the sections in this Annual Report entitled "Item 3. Key Information—D. Risk Factors" and "Item 5. Operating and Financial Review and Prospects" and elsewhere in this Annual Report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are organized under the laws of Ireland and our registered address is in Dublin, Ireland. In addition, all members of our Board of Directors, and all of our officers, as well as certain experts named herein, reside outside the United States. As a result, it may be difficult for investors to effect service of process within the United States upon us or such other persons residing outside the United States, or to enforce outside the United States judgments obtained against such persons in U.S. courts in any action, including actions predicated upon the civil liability provisions of the U.S. federal securities laws. In addition, it may be difficult for investors to enforce, in original actions brought in courts in jurisdictions located outside the United States, rights predicated upon the U.S. federal securities laws.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISORS

A. Directors and Senior Management

Not applicable.

B. Advisors

Not applicable.

C. Auditors

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

A. Offer Statistics

Not applicable.

B. Method And Expected Timetable

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

Our business is subject to a number of risks. You should carefully consider all of the information set forth in this Annual Report and in other documents we file with or furnish to the U.S. Securities and Exchange Commission, or SEC, including the following risk factors, before deciding to invest in or to maintain an investment in our securities. Our business, as well as our reputation, financial condition, results of operations, and share price, could be materially adversely affected by any of these risks, as well as other risks and uncertainties not currently known to us or not currently considered material.

Risk Factors Summary

Our ability to implement our business strategy is subject to numerous risks, as more fully described in this section. These risks include, among others:

- We are a clinical-stage biopharmaceutical company and we have incurred significant losses since our inception. We expect that we will continue to incur significant losses for the foreseeable future;
- We will need substantial additional funding, which may not be available on acceptable terms, or at all. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts;

- Preliminary, top-line or interim data from our clinical trials that we announce or publish from time to time may change as more data become available, and are subject to audit and verification procedures that could result in material changes in the final results or could otherwise harm our business, financial condition, results of operations and prospects;

- Drug and drug-device combination product development is a highly uncertain undertaking and involves a substantial degree of risk;

- GH001 and GH002 are investigational mebufotenin therapies based on a novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. To our knowledge, no such therapies have been approved in the United States or the EU for commercialization;

- Developing our proprietary aerosol delivery device for GH001 is a costly and uncertain process, and any failure of, or delay in, the development or manufacturing of the device may have a material adverse effect on our business and results of operations;

- Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome. The outcome of nonclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our currently completed clinical trials, which to date have only been conducted in Europe, and of our ongoing and future clinical trials, may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities;

- Our product candidates or use of our product candidates through participation in our clinical trials, may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences;

- GH001 and GH002, and any other product candidates we may develop, are subject to controlled substance laws and regulations in the territories where the product will be marketed, such as the United States, the EU and the rest of Europe, as well as the United Nations, or UN, international drug control treaties, and failure to comply with these laws and regulations, or the cost of compliance with these laws and regulations, may adversely affect the results of our business operations, both during clinical development and post-approval, and our financial condition. In addition, during the review process of GH001 and GH002, and prior to approval, the FDA, EMA and/or other comparable foreign regulatory authorities may require additional data, including with respect to whether GH001 or GH002 have abuse or misuse potential. This may delay approval and any potential rescheduling process;

- Mebufotenin is currently classified as a Schedule I drug in the United States and any product containing this substance, such as GH001 and GH002, must be rescheduled to be marketed. There can be no assurance that the Drug Enforcement Administration, or DEA, will make a favorable scheduling decision. Even assuming categorization as a Schedule II or lower controlled substance (i.e., Schedule III, IV or V) at the federal level, such substances would also require scheduling determinations under state laws and regulations;

- The potential reclassification of mebufotenin by the DEA in the United States could create additional regulatory burdens on our operations and negatively affect our results of operations;

- Our commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third-party payors and other members of the medical community;

- We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue;

- Our business and commercialization strategy depends on our ability to identify, qualify, prepare, certify, and support third-party clinics or treatment centers offering any of our product candidates, if approved. If we are unable to do so, our commercialization prospects would be limited and our business, financial condition, and results of operations would be harmed;

- We rely on patents, applications for patents and other intellectual property rights to protect our GH001 and GH002 product candidates, the prosecution, enforcement, defense and maintenance of which may be challenging and costly. Failure to adequately prosecute, maintain, enforce or protect these rights could harm our ability to compete and impair our business;

- We rely on third parties to assist in conducting our nonclinical studies and clinical trials. If they do not perform satisfactorily, we may not be able to initiate new clinical trials, successfully complete clinical trials, obtain regulatory approval or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed;

- The development and manufacture of our active pharmaceutical ingredients, product candidates and medical devices required to deliver such product candidates is complex, and we may encounter difficulties during further development or in production. We currently rely completely on third parties to develop, formulate and manufacture our nonclinical study and clinical trial supplies. The development and commercialization of any of our active pharmaceutical ingredients, product candidates and medical devices required to deliver such product candidates could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of such drug supplies or fail to do so at acceptable quality levels, including in accordance with rigorously enforced regulatory requirements or contractual obligations, and our operations could be harmed as a result;

- We depend heavily on our executive officers, principal consultants and others, and the loss of their services would materially harm our business;

- We previously identified and remediated material weaknesses in our internal control over financial reporting. If we experience additional material weaknesses or otherwise fail to maintain an effective system of internal controls in the future, our ability to accurately or timely report our financial condition or results of operations may be adversely affected; and

- We believe that we were a passive foreign investment company, or a PFIC, for our 2025 taxable year, and we anticipate that we will likely be a PFIC in 2026 and potentially also in future years, which could subject U.S. investors in our ordinary shares to significant adverse U.S. federal income tax consequences.

Risks Related to Our Financial Position and Need for Additional Capital

We are a clinical-stage biopharmaceutical company and we have incurred significant losses since our inception. We expect that we will continue to incur significant losses for the foreseeable future.

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval or become commercially viable. We have no products approved for commercial sale and have not generated any revenue to date, and we will continue to incur significant research and development and other expenses related to our clinical development and ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. Since our inception, we have devoted substantially all of our financial resources and efforts to research and development, including nonclinical studies, technical development and our clinical trials. Our financial condition and operating results, including net losses, may fluctuate significantly from quarter to quarter and year to year. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. Additionally, net losses and negative cash flows have had, and will continue to have, an adverse effect on our shareholders' equity and working capital. Our net losses were $48.3 million and $39.0 million for the years ended December 31, 2025 and 2024. As of December 31, 2025, we had an accumulated deficit of $154.4 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, our product candidates in our initial and any additional indications as well as for other product candidates.

We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials, including in expanded geographies such as the United States, for our GH001 and GH002 product candidates for our initial indications and any additional indications;
- continue both the technical development and expansion of our external manufacturing capabilities for our current product candidates GH001 and GH002 and of the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001;
- initiate and continue research and development, including technical, nonclinical, clinical, and discovery efforts for any future product candidates;
- seek to identify additional product candidates;
- seek regulatory approvals for our product candidates GH001 and GH002, including the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001, or any other product candidates that successfully complete clinical development;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate and device development and help us comply with our obligations as a public company;
- hire and retain additional personnel, such as clinical, quality control, scientific, commercial, sales, marketing and administrative personnel;
- continue to prepare, file, prosecute, maintain, protect and enforce our intellectual property rights and claims;
- establish sales, marketing, distribution, manufacturing, supply chain and other commercial infrastructure in the future to commercialize various products for which we may obtain regulatory approval;
- comply with ongoing regulatory requirements for products approved for commercial sale, if ever;
- adapt to ongoing changes in global economic conditions, including but not limited to continuing inflation, imposition of tariffs and trade barriers, interest rates and foreign currency exchange rates, disruptions in global supply chains and labor markets and geopolitical risks and global hostilities, including any direct or indirect economic impacts resulting from conflicts in Eastern Europe and the Middle East and the political, economic and social instability in Venezuela, tariff and trade wars, or increased tensions between China and Taiwan;
- acquire or in-license other product candidates, medical devices to deliver our product candidates, and other technologies; and
- incur increased costs as a result of operating as a public company.

Our expenses could increase beyond our expectations if we are required by the FDA or other comparable foreign regulatory authorities, to perform clinical trials in addition to those that we currently expect, or if there are any delays in establishing appropriate manufacturing arrangements for our product candidates or for the medical devices required to deliver our product candidates, or if there are any delays in completing our clinical trials or the development of any of our product candidates or of the medical devices required to deliver our product candidates.

We will need substantial additional funding, which may not be available on acceptable terms, or at all. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.

We expect to continue to spend substantial amounts to continue the technical, nonclinical and clinical development of our current and future programs. If we are able to gain marketing approval for product candidates that we develop, including any indication for which we are developing or may develop our GH001 and GH002 product candidates, we may require additional amounts of cash in order to launch and commercialize such product candidates and the medical devices required to deliver such product candidates to the extent that such launch and commercialization is not the responsibility of a future collaborator that we may contract with in the future. In addition, other unanticipated costs may arise in the course of our development efforts. Because the design and outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidates we develop, and changing circumstances, some of which may be beyond our control, such as heightened inflation and interest rates, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing our GH001 and GH002 product candidates, additional mebufotenin delivery approaches and the medical devices required to deliver these therapies, such as our proprietary aerosol delivery device for GH001, for our initial and any additional indications as well as other product candidates we may develop;
- the timing and uncertainty of, and the costs involved in, obtaining marketing approvals for our GH001 and GH002 product candidates including the medical devices required to deliver these therapies for our initial and any additional indications, and other product candidates we may develop and pursue;
- the number of future product candidates that we may pursue and their development requirements;
- the number of jurisdictions in which we plan to seek regulatory approvals;
- if approved, the costs of commercialization activities for GH001 and GH002 for any approved indications, or any other product candidate that receives regulatory approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution, and manufacturing capabilities;
- subject to receipt of regulatory approval, revenue, if any, received from commercial sales of GH001 and GH002 and the respective medical devices for any approved indications or any other product candidates;
- if approved, the establishment and maintenance of coverage and adequate reimbursement from third-party payors for GH001, GH002 or any other product candidates;
- the extent to which we may in-license or acquire rights to other products, product candidates, medical devices or technologies;
- our headcount growth and associated costs as we expand our research and development, increase our office space, and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications and maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property-related claims;
- the effect of competing product and market developments; and
- the ongoing costs of operating as a public company.

We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Any of our current or future license agreements may be terminated if we are unable to meet the payment or other obligations under the agreements.

Raising additional capital may cause dilution to holders of our ordinary shares, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We expect our expenses to continue to increase in connection with our planned operations. Until such time, if ever, that we can generate substantial product revenues, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, convertible debt financings, strategic collaborations and licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a shareholder. Debt financing, if available, may result in fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming shares or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through strategic collaborations or marketing, distribution, licensing and royalty arrangements with third parties, we may have to relinquish valuable rights to our intellectual property or technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us or issue and sell our shares, which may result in dilution to our shareholders. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We are in the early stages of clinical drug development and have a limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability. Since the number of patients included in our clinical trials is small and the follow-up is short, the results from such clinical trials may be less reliable than results achieved in larger clinical trials with longer follow-up, which may hinder our efforts to obtain regulatory approval for GH001, GH002 or any other product candidates.

We are a clinical-stage biopharmaceutical company with a limited operating history, focused on novel therapies which may be able to induce ultra-rapid and durable remissions in patients with depression and in other indications within our focus area of psychiatric and neurological disorders. We commenced operations in 2018, have no products approved for commercial sale, and have not generated any revenue from product sales. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. The results of clinical trials with smaller sample sizes, shorter follow-up and no concurrent control group, such as our completed Phase 1 clinical trial of GH001 in 22 healthy volunteers (GH001-HV-101), our completed Phase 1/2 clinical trial of GH001 in 16 patients with Treatment-Resistant Depression, or TRD (GH001-TRD-102), both with seven days follow-up, our completed Phase 1 clinical trial of GH001 in 46 healthy volunteers (GH001-HV-103) with thirty days follow-up, our Phase 2a proof-of-concept clinical trials of GH001 for the treatment of patients with bipolar II disorder, or BDII, and a current depressive episode (GH001-BD-202) and for the treatment of patients with postpartum depression, or PPD (GH001-PPD-203), and our Phase 1 clinical trial of GH002 in 64 healthy volunteers (GH002-HV-105) can each be disproportionately influenced by various biases associated with the conduct of small, uncontrolled, short-term clinical trials, such as the potential failure of the smaller sample size to accurately depict the features of the broader patient population, and the potential failure of shorter studies to accurately depict long-term safety and efficacy results, which limits the ability to generalize the results, thus making the clinical trial results less reliable than clinical trials with a larger number of patients and longer follow-up. As a result, there may be less certainty that such product candidate would achieve a statistically significant effect in any future clinical trials. If we conduct any future clinical trials of GH001 or GH002, we may not achieve a statistically significant result or the same level of statistical significance, if any, that we might have anticipated based on the results observed in our initial clinical trials. To date, our completed clinical trials have been conducted only in Europe, and we have not initiated nor completed a pivotal clinical trial, obtained marketing approval for any product candidates, manufactured a commercial scale product or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Our short operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

Due to the significant resources required for the development of our programs, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on programs that do not yield a successful product candidate or fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We currently have two product candidates in clinical development. The development of these programs and product candidates, of the medical devices required to deliver these product candidates and of any potential future programs and product candidates require significant capital investment. Due to the significant resources required for the development of our programs and product candidates, we must focus our programs and product candidates on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe there is the most evidence that we will be able to efficiently generate proof-of-concept data. We then intend to expand to clinical testing and seek regulatory approvals in other psychiatric and neurological disorders. However, even if any of our product candidates are able to gain regulatory approval in one indication, there is no guarantee that we will be able to expand to other indications, and we may expend significant resources in seeking such approvals.

In addition, we may focus resources on pursuing indications outside of psychiatric and neurological disorders based on the same strategic approach (e.g., mechanistic rationale, the availability of translational tools, clinical development path, commercial opportunity) we utilize in determining on which of our discovery programs to focus. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or particular medical devices to deliver those product candidates, or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Additionally, we have in the past and may in the future reprioritize product candidate development plans and activities and delay or terminate development of any product candidates we identify. Similarly, our potential decisions to delay, terminate, or collaborate with third parties in respect of certain programs, product candidates, or medical devices to deliver those product candidates may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, in particular for psychiatric and neurological disorders, our business, financial condition, and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

Failure of the U.S. federal government to manage its fiscal matters or to raise or further suspend the debt ceiling may expose us to increased financial and operational risk.

Congressional disagreement over the U.S. federal budget and the maximum amount of debt the federal government is permitted to have outstanding, often referred to as the debt ceiling, has previously caused the U.S. federal government to shut down for periods of time. Generally, if effective legislation to fund government operations and manage the level of federal debt is not enacted by the applicable deadline, the federal government may suspend its investments for certain government accounts, among other available options, in order to prioritize payments on its obligations. A failure by the U.S. Congress to pass spending bills or address the debt ceiling at any point in the future would increase the risk of default by the United States on its obligations, the risk of a lowering of the U.S. federal government's credit rating and the risk of other economic dislocations. Any such failure could also result in negative consequences for the Company. Potential impacts to our business may include:

- devaluation in U.S. government bond investments held by the Company;
- inability to access capital markets, or increased difficulty in doing so; or
- government shutdown, or reduced operation, of agencies such as the FDA, which could impede our ability to progress our planned IND and/or other U.S. operations.

Exchange rate fluctuations may materially affect our results of operations and financial condition.

Due to the international scope of our operations, our assets, earnings and cash flows are influenced by movements in exchange rates of several currencies, particularly the euro, the U.S. dollar and the pound sterling. Our consolidated financial results are presented in U.S. dollars, while the results of GH Research Ireland Limited, our subsidiary, are prepared in euro. Changes in exchange rates between the U.S. dollar and the euro will affect the translation of our GH Research Ireland Limited's financial results into U.S. dollars in reporting our consolidated results.

The majority of our operating expenses are paid in euro and pound sterling. Further potential future revenue may be derived from abroad, particularly from the United States. As a result, our business and the price of our ordinary shares may be affected by fluctuations in foreign exchange rates between the euro, the U.S. dollar and the pound sterling, which may also have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place. See Note 19 in the notes to our consolidated financial statements appearing elsewhere in this Annual Report for a description of foreign exchange risks.

In addition, the possible abandonment of the euro by one or more members of the EU could materially affect our business in the future. Despite measures taken by the EU to provide funding to certain EU member states in financial difficulties and by a number of European countries to stabilize their economies and reduce their debt burdens, it is possible that the euro could be abandoned in the future as a currency by countries that have adopted its use. This could lead to the reintroduction of individual currencies in one or more EU member states, or in more extreme circumstances, the dissolution of the EU. The effects on our business of a potential dissolution of the EU, the exit of one or more EU member states from the EU or the abandonment of the euro as a currency, are impossible to predict with certainty and any such events could have a material adverse effect on our business, financial condition and results of operations.

We have broad discretion over the use of our cash, cash equivalents and marketable securities, and may not use them effectively.

Our management has broad discretion to use our cash, cash equivalents and marketable securities to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our ordinary shares. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our ordinary shares to decline and delay the development of our product candidates. Pending our use to fund operations, we may invest our cash, cash equivalents and marketable securities in a manner that does not produce income or that loses value.

Risks Related to Research and Development and the Biopharmaceutical Industry

Preliminary, top-line or interim data from our clinical trials that we announce or publish from time to time may change as more data become available, and are subject to audit and verification procedures that could result in material changes in the final results or could otherwise harm our business, financial condition, results of operations and prospects.

From time to time we may publicly disclose preliminary, top-line, or interim data from our clinical trials, including the data we have disclosed for our current clinical trials. Preliminary and top-line data are based on an analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the preliminary or top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. This difference may be more pronounced because of the small sample size and short duration of our clinical trials. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously reported. We may also conduct planned interim analyses as part of our clinical trials before they are complete. Planned interim analyses from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. As a result, interim analyses, as well as preliminary or top-line data, should be viewed with caution until the final data are available. In addition, the data received from an interim analysis could prompt us to alter the trial design, or even to halt the clinical trial altogether. Finally, we may report interim, preliminary or top-line data of only certain endpoints rather than all endpoints. Adverse changes between interim, preliminary or top-line data and final data, or between the initially planned trial design and any subsequently altered elements of the trial design due to our analysis of interim, preliminary or top-line data, could significantly harm our business and prospects. Additional disclosure of interim, preliminary or top-line data, or of changes to the trial design, by us or by our competitors could result in volatility in the price of our ordinary shares.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the ability to initiate further clinical studies, the approvability or commercialization of the particular product candidate and our Company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the interim, preliminary or top-line data that we report differ from late, final or actual results, if we alter the trial design due to our analysis of interim, preliminary or top-line data, or if others, including the FDA, EMA or other comparable foreign regulatory authorities, disagree with the conclusions reached, our ability to initiate further clinical studies or obtain approval for, and commercialize our product candidates, may be harmed, which could harm our business, financial condition, results of operations and prospects.

Drug and drug-device combination product development is a highly uncertain undertaking and involves a substantial degree of risk.

We have no products approved for commercial sale. To generate revenues from the sales of any approved products that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing and marketing therapies with significant commercial success. Our ability to generate revenue and achieve profitability depends on many factors, including:

- completing research and technical, nonclinical and clinical development of our product candidates and the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001;
- obtaining regulatory approvals and marketing authorizations for product candidates, including the medical devices required to deliver these product candidates for which we successfully complete clinical development and clinical trials;
- developing a sustainable and scalable manufacturing process for our product candidates and the medical devices required to deliver these product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand of our product candidates and medical devices;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;

- successfully getting our product candidates rescheduled under the federal Comprehensive Drug Abuse Prevention and Control Act of 1970, also known as the Controlled Substances Act, or CSA, and comparable state laws by the DEA and other applicable regulatory agencies inside and outside the United States;
- launching and successfully commercializing product candidates and the medical devices required to deliver these product candidates for which we obtain regulatory approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining an adequate price for our product candidates and devices in the countries where our products are commercialized;
- obtaining coverage and adequate reimbursement for our product candidates and medical devices from payors;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- receiving milestone and other payments under any future collaboration arrangements;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- attracting, hiring and retaining qualified personnel; and
- complying with laws and regulations, including laws applicable to controlled substances, data privacy and pre-commercial activities.

Because of the numerous risks and uncertainties associated with drug and drug-device combination product development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever.

GH001 and GH002 are investigational mebufotenin therapies based on a novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. To our knowledge, no such therapies have been approved in the United States or the EU for commercialization.

We have concentrated our research and development efforts on GH001 and GH002 for the treatment of psychiatric or neurological disorders and our future success depends on our successful development of these product candidates. Our risk of failure is high. We may experience problems or delays in developing GH001 and GH002. Any such problems or delays would cause unanticipated costs, and any development problems may not be solved. For example, in September 2023, our IND for GH001 was placed on a clinical hold by the FDA requiring an inhalation toxicology study in a non-rodent species and an additional inhalation toxicology study. We completed the toxicology studies and met with the FDA, and the clinical hold was lifted by the FDA in December 2025. We cannot assure you that our existing and future INDs will not be subject to additional clinical holds, whether partial or full. In addition, we or another party may uncover a previously unknown risk associated with GH001 and/or GH002 that may be more problematic than we currently believe, and this may prolong the period of observation required for obtaining, or result in the failure to obtain, regulatory approval or may necessitate additional clinical testing. If we are not able to complete successful clinical trials on the schedule we expect, we will not be able to obtain regulatory approval, and will not be able to commercialize our product candidates, on the timelines we expect.

In addition, the product specifications and the clinical trial requirements of the FDA, the European Commission, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidate. The regulatory approval process for novel product candidates such as ours is unclear and can be more expensive and take longer than for other, better known or more extensively studied therapies. For example, because our GH001 and GH002 product candidates contain mebufotenin, which is categorized as a Schedule I controlled substance under the CSA, and is similarly categorized by most states, foreign governments and the UN Convention on Psychotropic Substances, 1971, the development towards regulatory approval of GH001 and GH002 is especially challenging and uncertain. The high technical complexity of the development of drug-device combination products further increases risks and uncertainties towards regulatory approval of our product candidates. This risk and uncertainty is particularly high in the area of drug-device combination products for inhaled delivery of the drug component, such as with GH001. In the past, drug-device combination products have experienced significant delays due to technical challenges faced in achieving the tight technical performance specifications required for regulatory approval, or due to specific adverse events associated with inhaled delivery. We anticipate that GH001 and the device required to deliver GH001 will require significant additional development work to allow regulatory approval. It is uncertain whether this development work will be successful. A similar context and similar risks apply to our GH002 product candidate. To our knowledge, no mebufotenin therapies have received FDA approval nor received marketing authorization from the European Commission. As a result, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for GH001 and GH002 in either the United States or the EU. Approvals by the European Commission may not be indicative of what the FDA may require for approval and vice versa.

Our business substantially depends upon the successful development of our GH001 and GH002 product candidates. Failure to successfully develop GH001 and/or GH002 would prevent us from obtaining regulatory approval for, and successful commercialization of, GH001 and/or GH002 and our business may be materially harmed.

We currently have no products approved for sale and invest the majority of our efforts and financial resources in the development of our lead product candidates, GH001 and GH002, for the treatment of psychiatric or neurological disorders. Successful continued development and ultimate regulatory approval of GH001 and GH002 for our initial and any additional indications is critical to the future success of our business. We will need to raise sufficient funds for, and successfully enroll and complete, our clinical development programs of our GH001 and GH002 product candidates for the treatment of TRD and potentially other psychiatric and neurological disorders.

Before we can generate any revenue from sales of GH001 and GH002 or any other approved product, we must undertake additional technical, nonclinical and clinical development, regulatory review and approval in one or more jurisdictions for the product candidates and the medical devices required to deliver these product candidates. To date, our completed clinical trials have been conducted exclusively in Europe. We plan to pursue clinical trials in additional European countries and the United States for all of our clinical programs. We do not expect that we need to submit separate Investigational Device Exemption applications, or IDEs, or other comparable applications, with the FDA for the medical devices, including our proprietary aerosol delivery device, that we use to deliver our product candidates, and we have not done so, though there can be no assurance that IDEs or comparable applications will not be necessary in the future. We also intend to seek regulatory approval for some or all of our product candidates outside of the United States, including the EU. We do expect separate applications to EU national member state authorities will be required for our proprietary aerosol delivery device for GH001 and may be required for other medical devices that we use to deliver our product candidates. Application requirements outside of the United States and the EU are less well understood at this time and separate applications may be needed. If the FDA or another comparable foreign regulatory authority were to conclude that any such medical device requires an IDE submission or a comparable application, it could delay or prevent us from utilizing such medical device in future trials. Even if we were to submit an IDE or a comparable application for the medical device, the FDA or other comparable foreign regulatory authorities may not grant necessary approvals requested by us in a timely manner, or at all. In addition, if one or more of our product candidates are approved, we must ensure access to sufficient commercial manufacturing capacity for the product candidates and the medical devices required to deliver these product candidates and conduct significant marketing efforts in connection with any commercial launch, as well as obtaining pricing and reimbursement authorizations in individual European and other countries. These efforts will require substantial investment, and we may not have the financial resources to continue development of our product candidates or commercialization of any products.

We may experience setbacks that could delay or prevent regulatory approval of our product candidates, including the medical devices to deliver our product candidates, such as our proprietary aerosol delivery device for GH001, or our ability to commercialize any products, including:

- delay or failure in establishing acceptable performance characteristics, quality manufacturing standards and manufacturing capabilities for our product candidates or for the medical devices required to deliver our product candidates;

- negative or inconclusive results from our nonclinical studies or clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional nonclinical testing or clinical trials or abandon a program;

- product or device-related side effects experienced by subjects in our clinical trials or by individuals using drugs or therapeutics similar to our product candidates;

- delays in submitting INDs (or IDEs, if applicable) in the United States or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or institutional review boards, or IRBs, to commence a clinical trial, including Schedule I research protocols required by the DEA, or a suspension or termination of a clinical trial once commenced;

- if the FDA, EMA or other comparable foreign regulatory authorities do not find the earlier technical, nonclinical and clinical trial work sufficient, then we may need to conduct additional technical development work or nonclinical or clinical trials beyond what we currently have planned, before we can initiate further clinical studies. Any significant technical development, nonclinical or clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our drug candidates and medical devices or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates and medical devices and may harm our business and results of operations;

- conditions imposed by the FDA, EMA or other comparable foreign regulatory authorities regarding the scope or design of our clinical trials;

- the FDA, EMA or other comparable foreign regulatory authorities may disagree with our clinical trial design, including with respect to dosing levels administered in our planned clinical trials, or the medical devices used to deliver our product candidates in the clinical trials, which may delay or prevent us from initiating our clinical trials with our originally intended trial design and the originally planned medical devices;

- delays in contracting with clinical trial sites or enrolling subjects in clinical trials, the inability to identify clinical trial sites willing to host our clinical trials and the required scheduled drug DEA researcher registration and Schedule I research protocol in the United States and similar licenses in other jurisdictions to be obtained and maintained by our clinical investigators;

- delays or interruptions in the supply of materials necessary for the conduct of our clinical trials;

- regulators, IRBs or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- the FDA, the EMA or other comparable foreign regulatory authorities may require us to submit additional data such as long-term toxicology studies or additional data for our product candidates or the medical devices required to deliver our product candidates;

- delays in reaching, or failure to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;

- our third-party contractors for nonclinical studies or clinical trials may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or take actions that could cause clinical trial sites or clinical investigators to drop out of the trial, which may require that we add new clinical trial sites or investigators;

- due to the impact of a pandemic, epidemic, outbreak of an infectious disease or a similar event, we may experience some delays and interruptions to our technical development efforts, nonclinical studies, clinical trials and/or regulatory approvals, we may experience delays or interruptions to our manufacturing supply chain, or we could suffer delays in reaching, or we may fail to reach, agreement on acceptable terms with third-party service providers on whom we rely;

- greater-than-anticipated clinical trial costs, including as a result of delays or interruptions that could increase the overall costs to finish our clinical trials as our fixed costs are not substantially reduced during delays;

- we may elect to, or regulators, IRBs, Data Safety Monitoring Boards, or DSMBs, or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- we may not have the financial resources available to begin and complete the planned trials, or the cost of clinical trials of any product candidates may be greater than we anticipate;

- the supply or quality of our product candidates, medical devices required to deliver our product candidates, or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate to initiate or complete a given clinical trial;

- inability to compete with other therapies;

- poor efficacy of our product candidates during clinical trials;

- failure to demonstrate an acceptable benefit/risk profile for our product candidates;

- inability to provide sufficient design, testing, manufacturing and quality information for the medical devices required to deliver our product candidates, including information to support their use and compatibility with the drug constituent of our product candidates;

- unfavorable FDA, EMA or other comparable foreign regulatory authority inspection and review of clinical trial sites or manufacturing facilities;

- if the DEA, or any state or other jurisdiction, delays rescheduling or fails to reschedule mebufotenin to Schedule II, III, IV or V, or delays classifying or fails to classify our product candidates to Schedule II, III, IV or V;

- unfavorable product labeling associated with any product approvals and any requirements for a Risk Evaluation and Mitigation Strategy, or REMS, that may be required by the FDA or comparable requirements in other jurisdictions to ensure the benefits of an individual product outweigh its risks;

- unfavorable acceptance of our product candidates or clinical trial data by the patient or medical communities or third-party payors;

- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;

- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular;

- varying interpretations of data by the FDA, EMA or other comparable foreign regulatory authorities; or
- we may experience cyber-attacks or other failures in our telecommunications or IT systems, or those of our collaborators, CROs, third-party logistics or other service providers, distributors, suppliers or other contractors or consultants.

We do not have complete control over many of these factors, including certain aspects of technical drug product and device development, nonclinical development, clinical development and the regulatory submission process, potential threats to our intellectual property rights and our manufacturing, marketing, distribution and sales efforts or that of any future collaborator.

GH001 is designed to deliver mebufotenin to the patient via inhalation of an aerosol into the lungs. This aerosol is defined by specific properties to be pharmaceutically acceptable, such as its purity, and to achieve efficient uptake of mebufotenin into the systemic circulation, such as its particle size distribution. The generation of this mebufotenin aerosol requires a drug product and a device with specific performance characteristics and properties, and it is therefore anticipated that GH001 and the specific device will be considered a drug-device combination product by the FDA, EMA or other comparable foreign regulatory authorities. For GH002, which is our intravenous mebufotenin formulation, such classification will depend on our final choice for its commercial presentation. Products that are considered to be drug-device combination products will require review and coordination by the drug and device centers within the FDA, or other comparable foreign regulatory authorities or notified bodies prior to initiation of clinical trials and prior to marketing approval, which may delay such trials or marketing approval. Under FDA regulations, combination products are subject to current good manufacturing practice, or cGMP, requirements applicable to both drugs and medical devices, including the Quality Management System, or QMS, and regulations applicable to medical devices. Combination products are also subject to the Medical Device Regulation 2017/745, or MDR, which requires coordination between the drug and the device regulatory laws and regulators. Problems associated with the drug product or device component of the combination product candidate may delay or prevent initiation of clinical trials or marketing approval. For example, in current and previous clinical trials, GH001 has been vaporized using a device we purchased on the market from a single third-party manufacturer, Storz & Bickel, Tuttlingen. We do not have a commercial supply agreement with Storz & Bickel, Tuttlingen. If the FDA, EMA or other comparable foreign regulatory authorities refuse to accept the use of this third-party device in our planned clinical trials then initiation of additional clinical trials could be significantly delayed or prevented. We also have not established licensing agreements with any alternative provider of a device which would be suitable to generate a pharmaceutically acceptable aerosol from GH001. In 2021, we initiated the development of a proprietary aerosol delivery device for GH001 for use in our pivotal clinical trial program and for commercial use. This development is not yet completed and if we fail to develop, manufacture, license, or acquire a device which would be suitable to generate a pharmaceutically acceptable aerosol from GH001, which achieves sufficient uptake of mebufotenin into the systemic circulation, or if we fail to get sufficient supplies of the third-party manufactured device or any alternative device or if the device is unavailable to us for any reason then initiation of additional clinical trials or receipt of marketing approval could be significantly delayed or prevented. If the manufacturer of the third-party device makes modifications, or if we elect to change a device component, or license an alternative device component, we will need to perform validation testing and obtain FDA, or other comparable foreign regulatory authority or notified body, approval prior to using the modified or alternative device or device component. Similar testing and validation would be required for our development of any proprietary devices. If the FDA or other comparable foreign regulatory or notified body fails to approve use of those modified or alternative medical devices or take significant enforcement action against the manufacturer, we would not be able to continue or initiate clinical trials, receive marketing approval or we may have to suspend marketing our products in certain jurisdictions.

In addition, of the large number of drugs in development in the biopharmaceutical industry, only a small percentage result in the submission of a marketing application, such as a new drug application, or NDA, to the FDA, EMA or other comparable foreign regulatory authority, and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval for GH001 or GH002, including the medical devices required for their administration, such as our proprietary aerosol delivery device for GH001, for any indication, any such approval may be subject to limitations on the indications or uses or patient populations for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure that we will successfully develop or commercialize GH001 or GH002 including the medical devices required for their administration, for any indication.

Developing our proprietary aerosol delivery device for GH001 is a costly and uncertain process, and any failure of, or delay in, the development or manufacturing of the device may have a material adverse effect on our business and results of operations.

The development process for our proprietary GH001 aerosol delivery device is incomplete. As a clinical-stage biopharmaceutical company, we do not have significant experience in manufacturing medical devices, or in working with a contract development and manufacturing organization, or CDMO, to manufacture medical devices, and as such we may not develop a device that is satisfactory either for our purposes or for necessary regulatory approvals. Further, a significant number of components in our proprietary aerosol delivery device for GH001 are manufactured in China, subjecting us to certain geopolitical risks, and other risks related to our supply chain, in manufacturing our device. See "Risks Related to Employee Matters, Managing Our Business and Operations—Our business is subject to economic, political, regulatory and other risks associated with international operations."

The regulatory pathway relating to approval of our device is highly complex as a result of the novelty of our device and the absence of established regulatory guidance applicable to our device presentation. The FDA, EMA, or other comparable foreign regulatory authorities, as applicable, may not accept our interpretation of existing guidance, which may impact the timelines for regulatory approval or result in a failure to obtain regulatory approval of our device at all.

Even if we ultimately develop a device that is suitable to generate a pharmaceutically acceptable aerosol and which achieves sufficient uptake of mebufotenin into the systemic circulation, and even if such device is approved, or exempt from approval requirements, as the case may be, by the FDA, EMA, or other comparable foreign regulatory authorities, there can be no assurance that we will be able to adequately manufacture such device in sufficient quantities, or at costs acceptable to us, or that third-party payors will adequately reimburse for them, to achieve our pre-commercial and commercial goals. Any such inability to adequately manufacture our device could materially delay our clinical trials or otherwise materially impact our business.

Further, our future success may depend in part on our ability to enhance our proprietary aerosol delivery device as well as develop or acquire new technologies to keep pace with technological developments, evolving industry standards and responses to changes in patient needs and expectations. A failure to adequately develop enhancements and improvements to our proprietary aerosol delivery device or acquire new devices that will address changing technologies and patient requirements adequately, or to introduce such devices on a timely basis, may have a material adverse effect on our clinical trials, business, financial condition and results of operations.

Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome. The outcome of nonclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our currently completed clinical trials, which to date have only been conducted in Europe and our ongoing and future clinical trials, may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities.

To obtain the requisite regulatory approvals to commercialize any product candidates and medical devices required for their administration, we must demonstrate through extensive nonclinical studies and clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. In particular, in the United States where we hope to advance our product development efforts in the future, the general approach for FDA approval of a new drug is dispositive data from two adequate and well-controlled Phase 3 clinical trials of the relevant drug in the relevant patient population, using the relevant device. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. A product candidate can fail at any stage of testing, even after observing promising signs of activity in earlier nonclinical studies or clinical trials. The results of nonclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Clinical trials with smaller sample sizes can be disproportionately influenced by various biases associated with the conduct of small clinical trials, making the clinical trial results less reliable than clinical trials with a larger number of patients. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to a lack of efficacy or emergence of unacceptable safety issues, notwithstanding promising results in earlier studies and trials. Also, a number of companies developing drug-device combination products, especially in the area of inhaled delivery of the drug component, have historically suffered significant setbacks due to technical, performance or manufacturing issues of the device component in their combination product. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of GH001, GH002 or any other product candidates. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- nonclinical studies or clinical trials may show the product candidates to be ineffective or less effective than expected (e.g., a clinical trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- failure to reflect similarly efficacious activity in subsequent clinical trials with larger patient populations;
- failure to use clinical endpoints that applicable regulatory authorities would consider clinically meaningful;
- manufacturing issues or formulation issues with the product candidate or device that cannot be resolved;
- failure to receive the necessary regulatory approvals;
- manufacturing issues, formulation issues, pricing or reimbursement issues or other factors that make a product candidate or device uneconomical; and
- intellectual property and proprietary rights of others and their competing products and technologies that may prevent one of our product candidates from being commercialized.

In particular, our nonclinical studies or clinical trials may show that our product candidates have unacceptable side effects or toxicities. In this context, our completed inhalation toxicology studies in rats showed certain respiratory tract histology findings. While these findings did not affect approval of our ongoing clinical trials in Europe, they prompted the FDA to request additional nonclinical studies to be completed before allowing us to initiate clinical studies in the United States. We completed the nonclinical studies and met with the FDA, and the clinical hold was lifted by the FDA in December 2025.

To date, we have assessed the intensity of psychoactive effect using a metric we devised, peak experience, or PE. We believe PE may correlate with clinical outcomes, but PE is a subjective metric, it can be inherently difficult to evaluate, and its psychometric validation has not yet been completed. It is uncertain if regulatory agencies will accept use of this metric to guide dosing in the context of the individualized dosing regimen, or IDR, in our pivotal program. In addition, differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials.

Moreover, our completed initial Phase 1 clinical trial of GH001 in healthy volunteers (GH001-HV-101), our completed Phase 1/2 clinical trial of GH001 in patients with TRD (GH001-TRD-102) and our completed Phase 2a proof-of-concept clinical trials of GH001 in BDII and a current depressive episode (GH001-BD-202) and in PPD (GH001-PPD-203) are open-label studies, where both the patient and investigator know whether the patient is receiving the product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the product candidate and sometimes do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. For example, prior major depressive disorder, or MDD, studies have exhibited a high placebo effect. In addition, open-label clinical trials may be subject to an “investigator bias,” where those assessing and reviewing the psychological and physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Therefore, it is possible that positive results observed in open-label trials will not be replicated in later placebo-controlled or active-controlled trials. Additionally, the trial design differences and placebo effects that may be possible in clinical research for the indications we are studying may make it difficult to extrapolate the results of earlier clinical trials to later clinical trials or to interpret the clinical data in any of our trials. Furthermore, even in a placebo-controlled or active-controlled trial, it is possible that patients and/or investigators will be able to discern if the administered dose is our product candidate or a placebo or the active control due to the psychoactive effects of mebufotenin, a phenomenon also known as functional unblinding. Therefore, placebo-controlled or active-controlled trials with our product candidates, such as our completed Phase 1 clinical trial of GH001 in healthy volunteers (GH001-HV-103), our completed Phase 2b clinical trial of GH001 in TRD (GH001-TRD-201) and our completed Phase 1 clinical trial of GH002 in healthy volunteers (GH002-HV-105) may be subject to similar limitations as open-label trials. Finally, our clinical trials to date have been short in duration, and our results may not be predictive of long-term safety and efficacy.

During the development and regulatory approval process for our product candidates, we engage in discussions with the FDA, the EMA and other comparable foreign regulatory authorities regarding our development programs, including discussions about the regulatory requirements for approval. As part of these discussions, different regulatory authorities may provide different or conflicting advice. While we attempt to harmonize the advice we receive from multiple regulatory authorities, it is not always practical to do so. Also, we may choose not to harmonize conflicting advice when harmonization would significantly delay clinical trial data or when we believe it is otherwise inappropriate. In addition, regulatory authorities may change their views on aspects of the clinical program, including study designs, or the ability of the studies as designed to support approval of a product candidate.

The standards that the FDA, EMA and other comparable foreign regulatory authorities use when regulating us require judgment and can change, which makes it difficult to predict with certainty how they will be applied. Although we are initially focusing our efforts on development of small molecule drug products and the medical devices required for delivery of these products, we may pursue development of other products, e.g., biological products, each of which could make us subject to additional regulatory requirements. Any analysis we perform of data from technical development, nonclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent initiation of clinical studies or regulatory approval. Our clinical trials have exclusively been conducted in Europe. The FDA's acceptance of data from clinical trials outside of the United States is subject to certain conditions. If the FDA or other comparable foreign regulatory authorities do not accept earlier technical, nonclinical or clinical data, we may need to conduct additional technical development, nonclinical studies or clinical trials. For example, our nonclinical data and device design verification information submitted with our GH001 IND was deemed by the FDA to contain insufficient information to assess risks to human subjects, and the FDA therefore requested additional nonclinical toxicology studies and other work (including acceptable device design verification information) before allowing us to initiate clinical studies in the United States. We completed the nonclinical and other studies and met with the FDA, and the clinical hold was lifted by the FDA in December 2025.

We may also encounter unexpected delays or increased costs due to new government regulations. Examples of such regulations include future legislation or administrative action, or changes in policy by the FDA, EMA or other comparable foreign regulatory authority during the period of product development and regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether regulations, guidance or interpretations of the FDA, EMA or other comparable foreign regulatory authority will be changed, or what the impact of such changes, if any, may be. In particular, in the United States, where we plan to develop our candidates in the future, the FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding on the FDA, may have a significant impact on our ability to obtain approval of any product candidates that we develop.

Successful completion of clinical trials is a prerequisite to submitting a marketing application to the FDA or other comparable foreign regulatory authorities for each product candidate and any relevant device required to deliver such product candidate, and, consequently, the ultimate approval and commercial marketing of any product candidates and medical devices. We may experience negative or inconclusive results, or regulators may be unwilling to accept nonclinical or clinical data obtained in foreign jurisdictions, which may result in our deciding, or our being required by regulators, to conduct additional clinical studies or trials or abandon some or all of our product development programs, which would have a material adverse effect on our business.

Even if we obtain regulatory approval with respect to GH001 for TRD, we may not be able to complete clinical development or obtain regulatory approval for additional indications, such as bipolar II disorder and postpartum depression, or we may be required to conduct trials in addition to those that we plan to conduct, which could limit our ability to realize the maximum market potential of GH001 or increase the costs of developing GH001 for any additional indications.

Given GH001's proposed mechanisms of resetting human brain functional connectivity, or FC, and serotonergic agonism, we believe that it represents a compelling therapeutic option for multiple psychiatric and neurological disorders other than TRD. Through collaborations with academic institutions and CROs we have begun to explore and intend to continue to explore the benefits of GH001 in additional psychiatric or neurological indications, the first of which have been BDII and PPD. However, there can be no assurance that, even if we obtain approval for GH001 for our initial indication, TRD, we will obtain approval for any other indication, including for BDII or PPD. The ability to obtain approval for any of these additional indications will require additional clinical development. If we fail to obtain and maintain required approvals for these additional or broadened indications, or if regulatory approvals are delayed, we will not realize the maximum market potential of GH001. Additionally, the FDA, EMA or other comparable foreign regulatory authorities may require us to conduct clinical trials, beyond those that we plan to conduct, and/or other tests, before seeking regulatory approval. For example, based on our existing nonclinical and clinical data for GH001, we believe that we can proceed to Phase 2a clinical trials in additional indications without first completing Phase 1 clinical trials, as we did with our Phase 2a proof-of-concept trials of GH001 in BDII and PPD. However, there can be no assurance that the FDA, EMA or other comparable foreign regulatory authorities will agree with such assessment. If we were required to conduct additional clinical trials and/or other tests, our costs for developing GH001 for any additional indications would be substantially higher and the timing of any regulatory approval, if any, would be substantially extended, which could adversely affect our results of operations.

We may not be able to submit INDs or IND amendments, or comparable foreign applications, to commence additional clinical trials on the timelines we expect, and even if we are able to do so, the FDA, EMA or comparable foreign regulatory authorities may not permit us to proceed.

In January 2026, we announced that the FDA had lifted the hold on our IND for GH001. However, we may not be able to submit INDs or comparable foreign applications for GH001, GH002 or for our other product candidates, on the timelines we expect. For example, we may experience delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND or a comparable foreign application will result in the FDA, EMA or a comparable foreign regulatory authority allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate clinical trials. For example, in September 2023, our IND for GH001 was placed on a clinical hold by the FDA requiring an inhalation toxicology study in a non-rodent species and an additional inhalation toxicology study. We provided the FDA with the requested information and met with the FDA, and the clinical hold was lifted by the FDA in December 2025. We cannot assure you that our existing and future INDs will not be subject to additional clinical holds, whether partial or full. Additionally, even if such regulatory authorities ultimately agree with the design and implementation of the clinical trials set forth in an IND or in a comparable foreign application, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND, or to comparable existing or new foreign applications. Any failure to submit INDs or comparable foreign applications on the timelines we expect, or to obtain permission for our trials to proceed, may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

Our product candidates or use of our product candidates through participation in our clinical trials may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Undesirable adverse drug reactions that could potentially be caused by GH001, GH002 or any other product candidate, and that have been observed in previously completed clinical trials, such as hypertension, tachycardia, nausea, vomiting, sensory disturbance, headache, flashbacks, referred to as the re-experiencing of some of the effects induced by mebufotenin intake at some point after the drug's acute effects have worn off, or that may potentially occur in ongoing or future studies, based on toxicities observed in completed nonclinical toxicity studies, such as serotonin syndrome, convulsions or respiratory adverse events, could cause us or regulatory authorities to not initiate, interrupt, delay or halt clinical trials and could result in more restrictive labeling than anticipated, a requirement that we implement a REMS to ensure that the benefits outweigh the risks or the delay or denial of regulatory approval by the FDA, EMA or comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics, even death. There can be no assurance that serious side effects, including deaths, will not occur even in the controlled setting of a clinical trial. In addition, many compounds that have initially shown promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevented further development of the compound. Additionally, the composition of our product candidates or learnings in nonclinical studies or clinical trials may result in contraindications or warnings, including "Boxed Warnings", for any product candidates for which we may obtain regulatory approval.

If unacceptable side effects arise in the development of our product candidates, foreign regulatory authorities, or, in the future, the FDA, EMA, the IRBs, DSMBs or independent ethics committees at the institutions in which our trials are conducted could refuse to allow us to initiate, or may suspend or terminate our nonclinical studies or clinical trials, or the FDA, EMA or other comparable foreign regulatory authorities could order us to cease nonclinical studies or clinical trials or deny approval of our product candidates for any or all targeted indications.

Treatment-emergent side effects that are deemed to be drug-related could also affect subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Undesirable side effects in one of our clinical trials for our product candidates in one indication could adversely affect enrollment in clinical trials, regulatory approval and commercialization of our product candidates in other indications. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, clinical trials of our product candidates are conducted in carefully defined sets of healthy volunteers and patients who have agreed to be enrolled in clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may fail to identify undesirable side effects. Clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients' use of the product candidate. If our product candidates, including the medical devices to deliver such product candidates, such as our proprietary aerosol delivery device for GH001, receive marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates or medical devices;
- regulatory authorities may require the addition of labeling statements, such as a "Boxed Warning" or contraindications;
- we may be required to change the way such product candidates are distributed or administered, or change the labeling of the product candidates or medical devices;
- the FDA may require a REMS to mitigate risks, which could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools, and regulatory authorities in other jurisdictions may require comparable risk mitigation plans;
- we may be subject to regulatory investigations and government enforcement actions;
- the FDA, EMA or a comparable foreign regulatory authority may require us to conduct additional technical development work or clinical trials or costly post-marketing testing and surveillance to establish and monitor the safety and efficacy of the product;
- we may be subject to litigation for injury caused to individuals exposed to or taking our product candidates or operating our medical devices; and
- our reputation may suffer.

In addition, patients who participate in our trials may take antidepressants or other medications to treat depression and/or mood disorders, or other medications that may interact with our product candidates, and participation in our clinical trials currently requires patients to suspend most of such existing medications or treatments for the duration of the trial. If a patient chooses to resume his or her existing medications, there is no guarantee such medications will produce the same therapeutic effect, if any, as may have been experienced prior to suspending such medication. Further, the impact of cycling off and/or back on to existing medications could have undesirable side effects or lead to severe mental health trauma. Any such negative reactions of a patient participating in one of our clinical trials may decrease the willingness of patients to participate in our trials, affect the timing or outcome of our clinical trials, product candidate development and approval process, or create negative public perception around our product candidates, which in turn may significantly impact our ability to successfully commercialize our product candidates.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates, could negatively impact the perception of our other product candidates, could substantially increase the costs of commercializing our product candidates, if approved, and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

If we encounter difficulties enrolling patients in our future clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion.

Patient enrollment is affected by many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- in the case of clinical trials focused on rare disease, the small size of the patient population and the potential of a patient being undiagnosed or misdiagnosed;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications that we are investigating;
- reluctance of physicians to encourage patient participation in clinical trials;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, including product candidates studying N-methyl-D-aspartate antagonists, neurosteroids, and mebufotenin and other serotonergic psychedelics such as psilocybin and N,N-dimethyltryptamine. This competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site, or which may lead to a bias in recruitment between the competing trials, potentially affecting the outcome of those trials.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Delays in patient enrollment may result in increased costs, affect the timing or outcome of the planned clinical trials, product candidate development and approval process and jeopardize our ability to seek and obtain the regulatory approval required to commence product sales and generate revenue, which could prevent completion of these trials, adversely affect our ability to advance the development of our product candidates, cause the value of our company to decline and limit our ability to obtain additional financing if needed.

We are also required to register certain clinical trials and post the results of certain completed clinical trials on a government-sponsored database, such as www.ClinicalTrials.gov in the United States and a similar system in the EU, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

The markets for GH001, GH002 and any other product candidates that we are developing or we may develop, for TRD or for any additional indications, may be smaller than we expect.

Our estimates of the potential market opportunity for GH001, GH002 and any other product candidates that we are developing or we may develop, for TRD or for any additional indications, include several key assumptions based on our industry knowledge, industry publications and third-party research reports. There can be no assurance that any of these assumptions are, or will remain, accurate. If the actual market for GH001, GH002 and any other product candidates that we are developing or we may develop, for TRD or for any additional indications, is smaller than we expect, our revenue, if any, may be limited and it may be more difficult for us to achieve or maintain profitability.

We may not be successful in our efforts to identify or discover additional product candidates in the future.

Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development or commercialization for a number of reasons, including:

- our inability to design such product candidates with the pharmacological or pharmacokinetic properties that we desire; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for nonclinical and clinical development, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact the market price of our publicly traded ordinary shares.

We may conduct clinical trials for our product candidates in the United States, Europe or other jurisdictions, and the FDA, EMA and applicable foreign regulatory authorities may not accept data from trials conducted outside those respective jurisdictions.

We may choose to conduct one or more of our clinical trials in the United States, Europe or in other foreign jurisdictions. The acceptance of study data from nonclinical studies and clinical trials conducted outside any such jurisdiction may be subject to certain conditions for acceptance. For example, in cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to Good Clinical Practices, or GCP, regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies, such as the EMA, have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. The FDA may not ultimately accept our data given the limited sample size in our completed and existing trials. For example, our completed clinical trials have exclusively been conducted in Europe. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

A Breakthrough Therapy Designation or a Fast Track Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

We do not currently have a Breakthrough Therapy Designation for any of our product candidates, but we may seek a Breakthrough Therapy Designation for any product candidate that we plan to develop in the United States if we believe the qualifying criteria for such a designation can be met. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA has discretion to determine whether the criteria for a Breakthrough Therapy has been met and whether to grant a Breakthrough Therapy Designation to a product candidate. Accordingly, even if we believe a product candidate we develop meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even after granting Breakthrough Therapy Designation to our product candidates, the FDA may later decide that the drugs no longer meet the conditions for qualification and withdraw the designation.

We do not currently have Fast Track Designation or acceptance of an accelerated assessment in the EU for any of our product candidates, but we may seek such a designation for the product candidates we plan to develop in the United States and the EU, if we believe the qualifying criteria for such a designation/ assessment have been met. If a product is intended for the treatment of a serious or life-threatening condition and nonclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for Fast Track Designation or accelerated assessment. The FDA and the EMA each have broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation/assessment, we cannot assure that the FDA or EMA would decide to grant it. Even if we do receive Fast Track Designation and or an accelerated assessment, we may not experience a faster development process, review or approval compared to conventional FDA or EMA procedures. The FDA or EMA may withdraw the Fast Track Designation or accelerated assessment, respectively, if either agency believes that the designation or pathway is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation and/or accelerated assessment have failed to obtain regulatory approval.

We may seek orphan drug designation for one or more of our product candidates in the United States, but we may be unable to obtain or maintain such a designation or the benefits associated with orphan drug status, including marketing exclusivity, which may cause our revenue, if any, to be reduced.

Because we are considering developing GH001 and/or GH002 for indications we believe to be rare, we may elect to pursue orphan designations for our candidates as applicable in the jurisdictions where development activities are planned.

In the United States, under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested and granted by the FDA before a new drug application, or NDA, is submitted. In the United States, orphan drug designation entitles a party to financial incentives such as tax advantages and user fee waivers. After the FDA grants orphan drug designation, it will disclose publicly the generic identity of the drug and its potential orphan use. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Such a designation may also be revoked by the FDA in certain circumstances, such as if the agency finds that the applicant’s request for designation request omitted material information required under the Orphan Drug Act and its implementing regulations.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity. This means that the FDA may not approve any other marketing applications for the same drug and the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan exclusivity or if the FDA finds that the holder of the orphan exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the drug was designated. Furthermore, the FDA can waive orphan exclusivity if the applicant is unable to manufacture sufficient supply of the product subject to a period of orphan drug marketing exclusivity.

We may seek orphan drug designation for one or more of our product candidates in the EU, but we may be unable to obtain or maintain such a designation or the benefits associated with orphan drug status, including marketing exclusivity, which may cause our revenue, if any, to be reduced.

In the EU, orphan designation might be granted by the EMA for a medicine that (i) is intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating; (ii) with a prevalence in the EU of not more than five in 10 thousand or it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development; and (iii) no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorized, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the EU, orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The benefit of orphan designation in the EU is scientific advice, and extended market exclusivity, or an additional two years on top of the eight years of market exclusivity for an innovative product. Such a designation may also be revoked by the EMA in certain circumstances, such as if the criteria are no longer met, which might for example occur by a competitor product becoming available in the market. Our inability to obtain or maintain such a designation or the benefits associated with orphan drug status could adversely affect our ability to achieve or sustain profitability.

Obtaining and maintaining regulatory approval of our product candidates and medical devices required to deliver such product candidates in one jurisdiction does not mean that we will be successful in obtaining or maintaining regulatory approval of our product candidates and medical devices required to deliver such product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates and medical devices required to deliver such product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants approval of a product candidate and device required to deliver such product candidate, comparable regulatory authorities in other jurisdictions, including Europe, must also approve the manufacturing, marketing and sale of the product candidate and device required to deliver such product candidate in those jurisdictions. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional nonclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate and device must also be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to governmental approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any partner we work with fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we, or any future collaborators, obtain regulatory approvals for our product candidates and medical devices to deliver such product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could impair our ability to generate revenue.

Once regulatory approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain regulatory approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we and any future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive regulatory requirements, including under FDA authorities ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any future collaborators and their contract manufacturers would be subject to periodic unannounced inspections by regulatory authorities to monitor and ensure compliance with cGMPs. Despite our efforts to inspect and verify regulatory compliance, one or more of our third-party manufacturing vendors may be found on regulatory inspection to be not in compliance with cGMP requirements, which may result in shutdown of the third-party vendor or invalidation of drug product lots or processes. In some cases, a product recall may be warranted or required, which would materially affect our ability to supply and market our drug products.

Accordingly, assuming we, or any future collaborators, receive regulatory approval for one or more of our product candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, or any future collaborators, are not able to comply with post-approval regulatory requirements, we, or any future collaborators, could have the regulatory approvals for our products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Changes in regulatory requirements, regulatory guidance or regulatory interpretations or unanticipated events during our nonclinical studies and clinical trials of our product candidates may occur, which may result in changes to nonclinical studies and clinical trial protocols or the need for additional nonclinical studies and clinical trials, which could result in increased costs to us and could delay our development timelines.

Changes in regulatory requirements, regulatory guidance or regulatory interpretations or unanticipated events during our nonclinical studies and clinical trials may force us to amend nonclinical studies and clinical trial protocols or the applicable regulatory authority may impose additional nonclinical studies and clinical trial requirements. Any changes in regulatory requirements, regulatory guidance or regulatory interpretations applicable to novel product candidates such as ours may be more likely to occur than any such changes applicable to other, better known or more extensively studied therapies. Amendments or changes to our clinical trial protocols would generally require resubmission to the applicable regulatory authority and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of clinical trials. These decisions may increase costs, and cause us not to meet expected timelines and, correspondingly, our business and financial prospects could be adversely affected. Similarly, amendments to our nonclinical studies may adversely impact the cost, timing or successful completion of those nonclinical studies. If we experience delays completing, or if we terminate, any of our nonclinical studies or clinical trials, or if we are required to conduct additional nonclinical studies or clinical trials, the development pathway, and ultimately the commercial prospects, for our product candidates may be harmed and our ability to generate product revenue from resulting products, if any, will be delayed.

We could be subject to product liability lawsuits based on the use of our product candidates in clinical testing or, if obtained, following our products' marketing approval and commercialization. Product liability lawsuits brought against us or any of our future collaborators could divert our resources and attention, require us to cease clinical testing, cause us to incur substantial liabilities or limit commercialization of our product candidates.

We are exposed to potential product liability risks that are inherent in the research, development, manufacturing, marketing and use of biopharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the use of our product candidates and medical devices to deliver such product candidates by us and any collaborators in clinical trials may expose us to liability claims. We will face an even greater risk if product candidates and medical devices to deliver such product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us, our suppliers, or our partners if any product candidate or medical devices to deliver such product candidates we develop allegedly causes injury or are found to be otherwise unsuitable for human use during product testing, manufacturing, marketing or sale. Any such product liability claim may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. Such claims could be made by participants enrolled in our clinical trials, patients, healthcare providers, biopharmaceutical companies, our collaborators or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources.

Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for any of our future approved products;
- injury to our reputation;
- initiation of investigations by regulators;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs;
- substantial monetary awards to, or costly settlements with, patients or other claimants;
- product recalls or a change in the indications for which any approved drug products may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, clinical development does not always fully characterize the safety and efficacy profile of a new medicine, and it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity associated with illness or other adverse effects resulting from physicians' or patients' use or misuse of our products or any similar products distributed by other companies.

We maintain product liability insurance coverage limited to clinical trial liability, and this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if we commercialize any product that receives regulatory approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product candidates that we seek to develop or commercialize from biopharmaceutical companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

Specifically, we face competition from 501(c)(3) non-profit medical research organizations, including the Usona Institute. Such non-profits may be willing to provide treatment at cost or for free, undermining our potential market for GH001, GH002 and any other product candidates we may develop. In addition, a number of for-profit biotechnology companies or institutions are specifically pursuing the development of mebufotenin or other tryptamines, such as psilocybin and N,N-dimethyltryptamine, to treat mental health illnesses, including TRD. These competitors include AtaiBeckley, COMPASS Pathways, Helus Pharma and Definium Therapeutics. In addition, an increasing number of companies are stepping up their efforts in discovery of new psychoactive compounds. It is also probable that the number of companies seeking to develop psychoactive products and therapies for the treatment of mental health illnesses, such as depression, will increase. If any of our competitors are granted an NDA for their therapies before us and manage to obtain approval for a broader indication, and thus access a wider patient population, we may face more intensified competition from such potential therapies and increased difficulties in winning market acceptance of our GH001 and GH002 product candidates or any other product candidates. All of these risks are heightened because mebufotenin, which is a known naturally occurring substance and therefore not subject to patent protection, may be deemed an appropriate substitute for GH001 and GH002.

We also face competition from larger and smaller pharmaceutical, biopharmaceutical and biotechnology companies who have developed or are developing therapies for the treatment of MDD and TRD, including Axsome Therapeutics. and will face future competition for any other indications we may seek to treat with our GH001 and GH002 product candidates. There are a number of companies that currently market and sell products or therapies, or are pursuing the development of products or therapies, for the treatment of depression, including antidepressants such as selective serotonin reuptake inhibitors, or SSRIs, and serotonergic norepinephrine reuptake inhibitors, or SNRIs, antipsychotics, cognitive behavioral therapy, or CBT, esketamine and ketamine, repetitive transcranial magnetic stimulation, or rTMS, electroconvulsive therapy, or ECT, vagus nerve stimulation, or VNS, deep brain stimulation, or DBS, N-methyl-D-aspartate antagonists, neurosteroids, and other serotonergic psychedelics such as psilocybin and N,N-dimethyltryptamine, among others. Many of these pharmaceutical, biopharmaceutical and biotechnology competitors have established markets for their therapies and have substantially greater financial, technical, human and other resources than we do and may be better equipped to develop, manufacture and market superior products or therapies. In addition, many of these competitors have significantly greater experience than we have in undertaking nonclinical studies and human clinical trials of new therapeutic substances and in obtaining regulatory approvals of human therapeutic products. Accordingly, our competitors may succeed in obtaining FDA, EMA or other comparable foreign regulatory authority approval for alternative or superior products. In addition, many competitors have greater name recognition and more extensive collaborative relationships. Smaller and earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

If any of these competitors or competitors for our other product candidates receive FDA, EMA or other comparable foreign regulatory authority approval before we do, our product candidates would not be the first treatment on the market, and our market share may be limited. In addition to competition from other companies targeting our target indications, any products we may develop may also face competition from other types of therapies.

Many of our current or potential competitors, either alone or with their strategic partners, have:

- greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;
- more extensive experience in nonclinical studies, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling drug products;
- more developed intellectual property portfolios;
- products that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

Mergers and acquisitions in the biopharmaceutical industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of our targeted disease indications or similar indications, which could give such products significant regulatory and market timing advantages over our product candidates. Our competitors also may obtain FDA, EMA or other comparable foreign regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product exclusivity from the FDA for indications that we are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Our inhalable GH001 mebufotenin product candidate is delivered via inhalation of aerosols produced by a vaporization device which is subject to device regulations in the United States and other jurisdictions. The FDA, EMA or other comparable foreign regulatory authorities, may not accept this device for clinical trials.

In current and previous clinical trials, GH001 has been vaporized using a device we have purchased on the market from a third party. This device has been used in previous trials, conducted by other parties with other products or product candidates, in Europe and the United States. However, there can be no assurance that the FDA or other comparable foreign regulatory authorities will allow it to be used with GH001 in future trials. In addition, we may decide in future clinical trials to use a different device than the one we have used previously, and the FDA or other comparable foreign regulatory authorities could similarly object to the use of any such device with GH001. For example, in 2021, we initiated the development of a proprietary aerosol delivery device for GH001 for use in our pivotal clinical trial program and for commercial use. We are in the process of completing an open-label Phase 1 trial to determine the pharmacokinetic, pharmacodynamics, and safety of GH001 administered via this proprietary aerosol delivery device in healthy subjects (GH001-HV-106). Any delays as a result of changing medical devices to deliver our product candidates would have a material adverse effect on our business.

We do not have a commercial supply agreement with the third-party manufacturer of the device we currently use in clinical trials, nor have we established license agreements with any alternative provider of a device that would be suitable to generate a pharmaceutically acceptable aerosol from GH001. There can be no assurance that the development of our proprietary aerosol delivery device will lead to a device that is suitable for our purpose, either in terms of efficacy or safety. If the FDA, EMA or other comparable foreign regulatory authorities refuse to accept the use of our proprietary aerosol device for GH001 in our planned clinical trials and if we fail to develop, manufacture, license, or acquire an alternative device which would be suitable to generate a pharmaceutically acceptable aerosol from GH001, or if we fail to get sufficient supplies of the current third-party device or any alternative device, then initiation of additional clinical trials or marketing approval could be significantly delayed or prevented.

Additional time may be required to obtain regulatory approval for GH001 because it is administered as a combination product.

GH001 is administered via inhalation of an aerosol produced by a vaporization device. This device is necessary to produce the aerosol and we therefore expect it to be regulated by the FDA as a drug-device combination product that requires coordination within the FDA, EMA or other comparable foreign regulatory authorities or notified bodies for review of their device and drug components. For GH002, which is our intravenous mebufotenin formulation, such classification will depend on our final choice for its commercial presentation. Medical products containing a combination of new drugs, biological products or medical devices may be regulated as "combination products" in the United States and Europe. A combination product generally is defined as a product comprised of components from two or more regulatory categories (e.g., drug/device, device/biologic, drug/biologic). Each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a new drug, biologic or device. In order to facilitate pre-market review of combination products, the FDA designates one of its centers to have primary jurisdiction for the pre-market review and regulation of the overall product based upon a determination by the FDA of the primary mode of action of the combination product. Where approval of the drug and device is sought under a single application, there could be delays in the approval process due to the increased complexity of the review process. The EMA has a parallel review process in place for combination products, the potential effects of which in terms of approval and timing could independently affect our ability to market our combination products in Europe.

Risks Related to Controlled Substances

GH001 and GH002, and any other product candidates we may develop, are subject to controlled substance laws and regulations in the territories where the product will be marketed, such as the United States, the EU and the rest of Europe, as well as the UN international drug control treaties, and failure to comply with these laws and regulations, or the cost of compliance with these laws and regulations, may adversely affect the results of our business operations, both during clinical development and post-approval, and our financial condition. In addition, during the review process of GH001 and GH002, and prior to approval, the FDA, EMA and/or other comparable foreign regulatory authorities may require additional data, including with respect to whether GH001 and GH002 have abuse or misuse potential. This may delay approval and any potential rescheduling process.

In the United States, mebufotenin is classified under the federal CSA and regulations as a controlled substance or scheduled substance, specifically as a Schedule I substance. The DEA regulates drug substances and chemical compounds as Schedule I, II, III, IV or V substances. Schedule I substances by definition have a high potential for abuse, have no currently "accepted medical use" in the United States, lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the United States. Pharmaceutical products approved for medical use in the United States may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. Schedule I and II drugs are subject to the strictest controls under the CSA, including manufacturing and procurement quotas, security requirements and import/export restrictions. In addition, prescribing and dispensing of Schedule II drugs is further restricted. For example, Schedule II prescriptions must contain a written signature or authorized e-signature and may not be refilled without a new prescription. Further, most, if not all, state laws in the United States classify mebufotenin as a Schedule I controlled substance. For any product containing mebufotenin to be available for commercial marketing in the United States, mebufotenin must be rescheduled to Schedule II, III, IV or V, or the DEA must reschedule a specific dosage form or product containing mebufotenin to Schedule II, III, IV or V. Similar rescheduling would be required in the various states and jurisdictions through scheduling-related legislative or administrative action.

Rescheduling determinations by the DEA to a schedule that would authorize the drug to be marketed (i.e., Schedule II, III, IV or V) are dependent on FDA approval of a substance or a specific formulation of a substance. Therefore, while mebufotenin is a Schedule I controlled substance, products approved by the FDA for medical use in the United States that contain mebufotenin would meet the statutory criteria to be placed in Schedule II, or another schedule, since approval by the FDA satisfies the "accepted medical use" requirement. If and when GH001 or GH002 receives FDA approval, the DEA will need to issue a proposed rulemaking to place mebufotenin in a schedule other than Schedule I in order for it to be prescribed to patients in the United States. This scheduling determination will be dependent on FDA approval and influenced by the FDA's recommendation as to the appropriate schedule. During the review process, and prior to approval, the FDA may determine that it requires additional data, either from nonclinical or clinical studies, including with respect to whether, or to what extent, the substance has the potential for abuse. This may introduce a delay into the approval and any potential rescheduling process because the scheduling process generally does not begin until approval. That delay would be dependent on the quantity of additional data required by the FDA. The scheduling determination will require the DEA to conduct notice and comment rulemaking. Such action will be subject to public comment and requests for an administrative hearing which could affect the timing and scheduling of these substances.

Mebufotenin is currently classified as a Schedule I drug in the United States and any product containing this substance, such as GH001 and GH002 must be rescheduled to be marketed. There can be no assurance that the DEA will make a favorable scheduling decision. Even assuming categorization as a Schedule II or lower controlled substance (i.e., Schedule III, IV or V) at the federal level, such substances would also require scheduling determinations under state laws and regulations.

If approved by the FDA, and if the finished dosage form of GH001 or GH002 is listed by the DEA as a Schedule II, III, or IV controlled substance, its manufacture, importation, exportation, domestic distribution, storage, sale, prescribing, and dispensing will continue to be subject to a significant degree of regulation by the DEA. In addition, the final scheduling process may take significantly longer than the 90-day deadline set forth in the CSA regarding an interim rule, especially if there are objections to such scheduling, thereby delaying the launch of our GH001 or GH002 product candidates in the United States. Furthermore, the FDA, DEA or any comparable foreign regulatory authority could require us to generate more clinical or other data than we currently anticipate to establish whether or to what extent the substance has an abuse, misuse or dependence potential, which could increase the cost and/or delay the launch of GH001, GH002 or any other product candidates containing controlled substances. In addition, product candidates containing controlled substances are subject to regulations relating to manufacturing, storage, distribution, prescribing, and dispensing, including:

- *DEA registration and inspection of facilities*. Facilities conducting research, manufacturing, distributing, importing or exporting, or dispensing controlled substances must be registered (licensed) to perform these activities and have the security, control, record keeping, reporting and inventory procedures required by the DEA to prevent drug loss and diversion. All these facilities must renew their registrations annually, except dispensing facilities (e.g. pharmacies), which must renew their registrations every three years. The DEA conducts periodic inspections of certain registered establishments that handle controlled substances. Failure to obtain or maintain the necessary registrations may result in delay of the importation, manufacturing or distribution of GH001 or GH002. Furthermore, importation of controlled substances is subject to additional permits or approvals, which must be obtained prior to each importation. Failure to comply with the CSA and implementing regulations promulgated by the DEA, particularly non-compliance resulting in theft, loss or diversion, can result in regulatory action that would have a material adverse effect on our business, financial condition and results of operations. The DEA and the U.S. Department of Justice may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to restrict, suspend or revoke those registrations. In certain circumstances, violations could lead to criminal proceedings.

- *State-controlled substances laws*. Individual U.S. states have also established controlled substance laws and regulations. Though state-controlled substances laws often mirror federal law, because the states are separate jurisdictions, they will need to separately reschedule GH001 or GH002. While some states automatically schedule or reschedule a drug based on federal action, other states schedule drugs through rule making or a legislative action. State scheduling may delay commercial sale of any product for which we obtain federal regulatory approval and adverse scheduling would have a material adverse effect on the commercial attractiveness of such product. We or our partners must also obtain separate state registrations, permits or licenses in order to be able to obtain, handle, and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions by the states in addition to those from the DEA or otherwise arising under federal law.

- *Clinical trials*. Because our GH001 and GH002 product candidates contain mebufotenin, to conduct clinical trials with GH001 and GH002 in the United States prior to approval, each of our research sites must submit a research protocol to the DEA and obtain and maintain a DEA Schedule I researcher registration that will allow those sites to handle and dispense GH001 and GH002 and to obtain the product from our importer. If the DEA delays or denies the grant of a researcher registration or approval of the research protocol to one or more research sites, the clinical trial could be significantly delayed, and we could lose clinical trial sites. The importer for the clinical trials must also obtain a Schedule I importer registration and an import permit for each import.

- *Post-Approval Importation*. If GH001 or GH002 is approved and classified as a Schedule II, III or IV substance, an importer can import it for commercial purposes if it obtains an importer registration and applies for and receives an import permit (Schedule II) or files an import declaration (Schedule III or IV) for each import shipment. The DEA provides annual assessments/estimates to the UN International Narcotics Control Board, which guides the DEA in the amounts of controlled substances that the DEA authorizes to be imported. The failure to identify an importer or obtain the necessary import authority, including specific quantities, could affect the availability of GH001 or GH002 and have a material adverse effect on our business, results of operations and financial condition. In addition, an application for a Schedule II importer registration must be published in the Federal Register, and there is a notice and comment period to receive public comments. It is always possible that adverse comments may delay the grant of an importer registration. If GH001 or GH002 is approved and classified as a Schedule II controlled substance, federal law may prohibit the import of the substance for commercial purposes. If GH001 or GH002 is listed as a Schedule II substance, we will not be allowed to import the drug for commercial purposes unless the DEA determines that domestic supplies are inadequate or there is inadequate domestic competition among domestic manufacturers for the substance as defined by the DEA. Moreover, the DEA has not registered any companies to import Schedule I controlled substances, including mebufotenin, for commercial purposes, only for scientific and research needs. Therefore, if neither GH001 or GH002, nor its drug substance could be imported, GH001 and GH002 would have to be wholly manufactured in the United States, and we would need to secure a manufacturer that would be required to obtain and maintain a separate DEA registration for that activity.

- *Manufacture in the United States*. If, because of a Schedule II (and possibly Schedule III) classification or voluntarily, we were to conduct manufacturing or repackaging/relabeling in the United States for commercial purposes, mebufotenin will be subject to an annual aggregate production quote established by the DEA and our contract manufacturers would be subject to the DEA's annual and semi-annual manufacturing and procurement quota requirements. Additionally, regardless of the scheduling of GH001 or GH002, the active ingredient in the final dosage form is currently a Schedule I controlled substance and would be subject to such quotas as this substance could remain listed on Schedule I during the clinical trials. The annual and semi-annual quota allocated to us or our contract manufacturers for the active ingredient in GH001 or GH002 may not be sufficient to complete clinical trials or meet commercial demand. Consequently, any delay or refusal by the DEA in establishing our, or our contract manufacturers', procurement and/or production quota for controlled substances could delay or stop our clinical trials or product launches, which would have a material adverse effect on our business, financial position and results of operations.

- *Distribution in the United States*. If GH001 or GH002 is scheduled as Schedule II, III, IV or V, we would also need to identify wholesale distributors with the appropriate DEA registrations and authority to distribute GH001, GH002 and any other product candidates. These distributors would need to maintain Schedule II, III, IV or V distribution registrations. This limitation in the ability to distribute GH001 or GH002 more broadly may limit commercial uptake and could negatively impact our prospects. The failure to obtain, or delay in obtaining, or the loss of any of those registrations could result in increased costs to us. If GH001 or GH002 is classified as a Schedule II drug, participants in our supply chain may have to maintain enhanced security including specially constructed vaults at manufacturing and distribution facilities. This additional security may also discourage some pharmacies from carrying the product. In addition, GH001 and/or GH002 could be required to be administered at our trial sites or other certified healthcare settings, which could limit commercial uptake. Furthermore, state and federal enforcement actions, regulatory requirements, and legislation intended to reduce prescription drug abuse, such as the tracking of prescribing and dispensing of controlled substances through a state prescription drug monitoring program, may make physicians less willing to prescribe, and pharmacies to dispense, certain controlled substances, especially Schedule II products.

The potential reclassification of mebufotenin by the DEA in the United States could create additional regulatory burdens on our operations and negatively affect our results of operations.

If mebufotenin, rather than just a specific FDA-approved formulation, is rescheduled under the CSA as a Schedule II or lower controlled substance (i.e., Schedule III, IV or V), the ability to conduct research on mebufotenin would most likely be improved. However, rescheduling mebufotenin may materially alter enforcement policies across many federal and state agencies, primarily the FDA and DEA. The FDA is responsible for ensuring public health and safety through regulation of food, drugs, supplements, and cosmetics, among other products, through its enforcement authority pursuant to the Federal Food, Drug, and Cosmetic Act, or FDCA. The FDA's responsibilities include regulating the ingredients as well as the marketing and labeling of drugs sold in interstate commerce. Because it is currently illegal under federal law to produce and sell mebufotenin, and because there are no federally recognized medical uses, the FDA has historically deferred enforcement related to mebufotenin to the DEA. If mebufotenin were to be rescheduled to a federally controlled, yet legal, substance, the FDA would likely play a more active regulatory role. The DEA would continue to be active in regulating manufacturing, distribution and dispensing of such substances. The potential for multi-agency enforcement post-rescheduling, including state agencies, e.g., Boards of Pharmacy, could threaten or have a materially adverse effect on our business.

GH001 and GH002 contain controlled substances, the use of which may generate public controversy. Adverse publicity or public perception regarding mebufotenin and psychedelics generally or our current or future product candidates using mebufotenin may negatively influence the success of these therapies.

Therapies containing controlled substances may generate public controversy. Political and social pressures and adverse publicity could lead to delays in approval of, and increased expenses for, GH001, GH002 and any other product candidates we may develop. Opponents of these therapies may seek restrictions on marketing and withdrawal of any regulatory approvals. In addition, these opponents may seek to generate negative publicity in an effort to persuade the medical community to reject these therapies. For example, we may face media-communicated criticism directed at our clinical development program. Adverse publicity from mebufotenin misuse may adversely affect the commercial success or market penetration achievable by our GH001 and GH002 product candidates. Anti-psychedelic protests have historically occurred and may occur and generate media coverage. Political pressures and adverse publicity could lead to delays in, and increased expenses for, and limit or restrict the introduction and marketing of, GH001, GH002 or any other product candidates.

If GH001, GH002 or any other product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of the safety and quality of our therapies. We may face limited adoption if third-party therapy sites, therapists, and patients are unwilling to try such a novel treatment. Even if therapies containing controlled substances become widely accepted by physicians and patients, our success will depend in large part on our ability to educate and train physicians and patients, and to successfully demonstrate the safety, tolerability, ease of use, efficacy, cost effectiveness and other advantages of therapies containing controlled substances. There has been a history of negative media coverage regarding psychedelic substances, including mebufotenin, which may affect the public's perception of our therapies. In addition, mebufotenin elicits intense psychological experiences, and this could deter patients from choosing this course of treatment. We could be adversely affected if we were subject to negative publicity or if any of our therapies or any similar therapies distributed by other companies prove to be, or are asserted to be, harmful to patients. Because of our dependence upon consumer perception, any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our therapies or any similar therapies distributed by other companies could have a material adverse impact on our business, prospects, financial condition and results of operations.

Future adverse events in research into depression and mental health diseases on which we focus our research efforts, or the pharmaceutical industry more generally, could also result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approvals of our therapies. Any increased scrutiny could delay or increase the costs of obtaining regulatory approval for GH001, GH002 or any other product candidates.

Mebufotenin is listed as a Schedule I controlled substance under the CSA in the United States, and comparable controlled substance legislation in other countries and the UN Convention on Psychotropic Substances, 1971, and any significant breaches in our compliance with these laws and regulations, or changes in the laws and regulations may result in interruptions to our development activity or business continuity.

Mebufotenin is categorized as a Schedule I controlled substance under the CSA, and is similarly categorized by most states, foreign governments and the UN Convention on Psychotropic Substances, 1971. Even assuming that GH001, GH002 or any other product candidates containing mebufotenin in specific formulations or dosage forms are approved and scheduled by regulatory authorities to allow their commercial marketing, the active pharmaceutical ingredients in such product candidates would likely continue to be Schedule I, or the state or foreign equivalent. Violations of any federal, state or foreign laws and regulations could result in significant fines, penalties, administrative sanctions, convictions or settlements arising from civil proceedings conducted by either the federal government or private citizens, or criminal charges and penalties, including, but not limited to, disgorgement of profits, cessation of business activities, divestiture, or prison time. This would have a material adverse effect on us, including on our reputation and ability to conduct business, the potential listing of our ordinary shares, our financial position, operating results, profitability or liquidity or the market price of our ordinary shares. In addition, it is difficult for us to estimate the time or resources that would be needed for the investigation or defense of any such matters or our final resolution because, in part, the time and resources that may be needed are dependent on the nature and extent of any information requested by the applicable authorities involved, and such time or resources could be substantial. It is also illegal to aid or abet such activities or to conspire or attempt to engage in such activities. An investor's contribution to and involvement in such activities may result in federal civil and/or criminal prosecution, including, but not limited to, forfeiture of his, her or its entire investment, fines and/or imprisonment.

Various federal, state, provincial and local laws govern our business in the jurisdictions in which we operate or currently plan to operate, and to which we export or currently plan to export our products, including laws relating to health and safety, the conduct of our operations, and the production, storage, sale and distribution of our products. Complying with these laws requires that we comply concurrently with complex federal, state, provincial and/or local laws. These laws change frequently and may be difficult to interpret and apply. To ensure our compliance with these laws, we will need to invest significant financial and managerial resources. It is impossible for us to predict the cost of such laws or the effect they may have on our future operations. A failure to comply with these laws could negatively affect our business and harm our reputation. Changes to these laws could negatively affect our competitive position and the markets in which we operate, and there is no assurance that various levels of government in the jurisdictions in which we operate will not pass legislation or regulation that adversely impacts our business.

In addition, even if we or third parties were to conduct activities in compliance with U.S. state or local laws or the laws of other countries and regions in which we conduct activities, potential enforcement proceedings could involve significant restrictions being imposed upon us or third parties, while diverting the attention of key executives. Such proceedings could have a material adverse effect on our business, revenue, operating results and financial condition as well as on our reputation and prospects, even if such proceedings conclude successfully in our favor. In the extreme case, such proceedings could ultimately involve the criminal prosecution of our key executives, the seizure of corporate assets, and consequently, our inability to continue business operations. Strict compliance with state and local laws with respect to mebufotenin does not absolve us of potential liability under U.S. federal law, or of the laws of EU member states, nor provide a defense to any proceeding which may be brought against us. Any such proceedings brought against us may adversely affect our operations and financial performance.

Despite the current status of mebufotenin as a Schedule I controlled substance in the United States, there may be changes in the status of mebufotenin under the laws of certain U.S. states. The legalization of mebufotenin without regulatory oversight may lead to the setup of clinics without proper therapeutic infrastructure or adequate clinical research, which could put patients at risk and bring reputational and regulatory risk to the entire industry, making it harder for us to achieve regulatory approval. Furthermore, the legalization of mebufotenin could also impact our commercial sales if we receive regulatory approval as it would reduce the barrier to entry and could increase competition.

Risks Related to the Commercialization of our Product Candidates

Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Even if the FDA or a comparable foreign regulatory authority approves any of our product candidates and the medical devices required to deliver such product candidates, we will be subject to ongoing regulatory requirements in the applicable jurisdictions for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and their facilities are required to comply with extensive regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates and the medical devices required to deliver such product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. In the United States, the FDA may also require a REMS as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

In the United States, the FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information or other restrictions; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the manufacturing of our products, the approved manufacturers or the manufacturing process;
- withdrawal of the product from the market or voluntary product recalls;
- requirements to conduct post-marketing studies or clinical trials;
- fines, restitution or disgorgement of profits or revenues;
- warning or untitled letters from the FDA or comparable notice of violations from comparable foreign regulatory authorities;
- suspensions of any of our ongoing clinical trials;
- refusal by the FDA or other comparable foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of marketing approvals;
- product seizure or detention or refusal to permit the import or export of products; and
- consent decrees, injunctions or the imposition of civil or criminal penalties.

Regulatory authorities strictly regulate marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, in the United States, companies may share truthful and not misleading information that is not inconsistent with the labeling. The FDA and other comparable foreign regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Violations of the FDCA relating to the promotion of prescription drugs may also lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws. Accordingly, to the extent we receive marketing approval for one or more of our product candidates, we and our third-party partners will continue to expend time, money and effort in all areas of regulatory compliance, including promotional and labeling compliance, manufacturing, production, product surveillance and quality control.

The policies of the FDA or other comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow to, or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Our commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third-party payors and other members of the medical community.

Even if any of the product candidates we develop receives marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, such as Medicare and Medicaid programs and managed care organizations in the United States, and others in the medical community. In addition, the availability of coverage and adequacy of reimbursement by third-party payors may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our products, if approved, for sale at competitive prices;
- relative convenience and ease of administration compared to alternative treatments;
- perceptions by the medical community, physicians, and patients, regarding the safety and effectiveness of our products and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the size of the market for such product candidate, based on the size of the patient subsets that we are targeting, in the territories for which we gain regulatory approval;
- the recommendations with respect to our product candidates in guidelines published by various scientific organizations applicable to us and our product candidates;
- the strength of sales, marketing and distribution support;
- the timing of any such marketing approval in relation to other product approvals;
- any restrictions on concomitant use of other medications;
- support from patient advocacy groups;

- media coverage regarding psychedelic substances;
- the ability to obtain sufficient third-party coverage and adequate reimbursement from government and third-party payors; and
- the prevalence and severity of any side effects.

If government and other third-party payors do not provide coverage and adequate reimbursement levels for any products we commercialize, market acceptance and commercial success would be reduced.

The successful commercialization of our product candidates in the United States will depend in part on the extent to which third-party payors, including governmental authorities and private health insurers, provide coverage and adequate reimbursement levels, as well as implement pricing policies favorable for our product candidates. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States and in other countries, patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. The availability of coverage and adequacy of reimbursement for our products by third-party payors, including government healthcare programs (e.g., Medicare, Medicaid, TRICARE), managed care providers, private health insurers, health maintenance organizations and other organizations is essential for most patients to be able to afford medical services and biopharmaceutical products such as our product candidates. Third-party payors decide which medications they will pay for and establish reimbursement levels.

In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent our products will be covered and reimbursed under Medicare. Although private third-party payors tend to follow Medicare practices, no uniform or consistent policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor as well as from state to state. Consequently, the coverage determination process is often a time-consuming and costly process that must be played out across many jurisdictions and different entities and that will require us to provide scientific, clinical and health economics support for the use of our products compared to current alternatives and do so to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained and in what time frame. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for our products and related treatments will be available from third-party payors. Moreover, the process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product, and a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates.

A decision by a third-party payor not to cover or not to separately reimburse for our medical products or therapies using our products could reduce physician utilization of our products once approved. Assuming there is coverage for our product candidates, or therapies using our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States will be available for our current or future product candidates, or for any procedures using such product candidates, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

Further, increasing efforts by third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost effectiveness of our products, in addition to the costs required to obtain FDA, EMA or other comparable foreign regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third-party payors in connection with the potential sale of any of our product candidates.

Our business and commercialization strategy depends on our ability to identify, qualify, prepare, certify, and support third-party clinics or treatment centers offering any of our product candidates, if approved. If we are unable to do so, our commercialization prospects would be limited and our business, financial condition, and results of operations would be harmed.

Our commercial success with GH001, GH002 or any other product candidates, if approved, will be dependent upon our ability to identify, qualify, prepare, certify, and support third-party clinics or treatment centers that administer our product candidates. We expect that GH001, GH002 and any other product candidates will be administered in qualified third-party clinics or treatment centers by certified healthcare providers. Because we intend to work with third-party centers and providers who agree to adhere to our treatment protocols, possibly under a REMS in the United States or a Risk Management Program, or RMP, in Europe with restricted distribution methods, we may face limitations on the number of sites available to administer GH001, GH002 or other product candidates. Moreover, sites may have difficulty satisfying the requirements of any REMS or RMP. Any limitations on the sites available to administer GH001, GH002 or other product candidates could make it impracticable or impossible for some potential patients to access our product candidates, if approved, which could limit the overall size of our potential patient population and harm our future results of operations.

If we are unable to establish or collaborate with a sufficient network of third-party clinics or treatment centers certified under applicable standards, including regional, national, state or other applicable standards as needed to administer GH001, GH002 or any other product candidate, including the certifications that such third-party clinics or treatment centers may require under a potential REMS in the United States or RMP in Europe, it would have a material adverse effect on our business and ability to grow and would adversely affect our results of operations and commercialization efforts.

Given the novel nature and scheduled drug aspect of our treatment, third-party clinics or treatment centers may face additional financial and administrative burdens in order to deliver any approved therapy, including adhering to a REMS in the United States or an RMP in Europe. The process for a third-party clinic or treatment center to comply with a REMS can be costly and time-consuming, which could delay a third-party clinic or treatment centers' ability to administer our product candidates and materially adversely affect our commercialization trajectory. Furthermore, third-party clinics or treatment centers will need to ensure that they have the necessary infrastructure and equipment in order to deliver GH001, GH002 or any other product candidates, such as adequate ancillary equipment and sufficient treatment rooms. This may deter third-party clinics or treatment centers from providing GH001, GH002 or any other product candidates and reduce our ability to expand our network and generate revenue.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. Some countries have a separate decision-making process in addition to whether the government or state insurers will reimburse the price for the product. The requirements governing drug pricing vary widely from country to country. For example:

- in the EU, member states can restrict the range of medicinal products for which their national health insurance systems provide reimbursement and, in most EU countries, the prices of medicinal products for human use must be approved by national health authorities, before they may be supplied;

- a common criterion relied upon by almost all EU Member States for pricing decisions is international reference pricing (the methodology and weight to be attached varies between countries);

- in many countries in Europe, prices of branded medicines must be notified or approved prior to product launch;

- reimbursement decisions in EU/European Economic Area, or EEA, are typically based on various forms of health technology assessment, including cost effectiveness determinations. From 2025, the EU's Health Technology Assessment Regulation (Regulation (EU) 2021/2282), or HTA Regulation, will start to come into effect providing for a common assessment of clinical effectiveness to be taken into account by national reimbursement authorities across EU/EEA; and

- additionally public procurement tenders are widely used for purchasing of medicinal products by hospitals.

Even if we obtain approval of any of our product candidates in the United States or Europe, we may never obtain approval or commercialize such products in other countries, which would limit our ability to realize their full market potential.

In order to market any products in the United States or Europe we must establish and comply with numerous and varying regulatory requirements regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals outside of where our clinical trials currently have been conducted could result in significant delays, difficulties and costs for us and may require additional nonclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time-consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue.

We have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our product candidates ultimately receives regulatory approval, we expect to establish a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming. We have no prior experience as a company in the marketing, sale and distribution of biopharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may also choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

Risks Related to Ongoing Regulatory and Legal Compliance

Changes and uncertainties in the tax system in the countries in which we have operations could materially adversely affect our financial condition and results of operations, and reduce net returns to our shareholders.

We plan to conduct business globally and may file income tax returns in multiple jurisdictions in the future. Our consolidated effective income tax rate could be materially adversely affected by several factors, including: changing tax laws, regulations and treaties, or the interpretation thereof; tax policy initiatives and reforms under consideration (such as those related to the Organization for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the OECD's Pillar One and Pillar Two initiatives (as discussed below) and other initiatives); the practices of tax authorities in jurisdictions in which we operate; the resolution of issues arising from tax audits or examinations and any related interest or penalties. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid.

We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices in jurisdictions in which we operate, could increase the estimated tax liability that we have expensed to date and paid or accrued on our balance sheets, and otherwise affect our financial position, future results of operations, cash flows in a particular period and overall our effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders and increase the complexity, burden and cost of tax compliance. On October 7, 2021, the Irish Government approved Ireland's adherence to the OECD BEPS 2.0 plan, under the OECD Inclusive Framework, to reform international tax rules. The OECD BEPS 2.0 plan consists of two distinct limbs; Pillar One and Pillar Two. On December 20, 2021, as part of the BEPS 2.0 plan, the OECD published the draft Global Anti-Base Erosion Model Rules (Pillar Two), or GloBE Rules, which are aimed at ensuring that Multinational Enterprises, or MNEs, with revenue of more than €750 million annually will be subject to a global minimum 15% effective tax rate. A directive to implement the GloBE Rules in the EU was adopted by the Council of the EU on December 15, 2023. Pillar Two was implemented into Irish law with effect for periods beginning on or after December 31, 2023. On October 11, 2023, the OECD released a package of documents in relation to Amount A of Pillar One, including a Multilateral Convention. Amount A of Pillar One, if implemented in its current form, would re-allocate certain profits of large multi-national groups to the jurisdictions where their customers and users are located and would apply to groups with revenues of above €20 billion and profitability exceeding 10% (or, if a group is below those thresholds but has a particular segment of its business as disclosed in its consolidated financial statements, a Disclosed Segment, which exceeds those thresholds, the rules may apply to that Disclosed Segment). In order for this Multilateral Convention to enter into force, it must be ratified by at least 30 jurisdictions including the headquarters of jurisdictions of at least 60% of MNEs that are currently expected to be within the scope of Amount A.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, or may apply existing rules in an unforeseen manner, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken or will take, which could result in increased tax liabilities. For example, The Office of the Revenue Commissioners of Ireland, or Revenue, or another tax authority could challenge our potential future allocation of income by tax jurisdiction and the amounts paid between potential future affiliated companies pursuant to potential future intercompany arrangements and transfer pricing policies, including amounts to be paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. Additionally, a tax authority could assert that we are tax resident in a jurisdiction where we believe we are not. A change of tax residency could subject us to a higher tax rate or an exit tax.

A tax authority may take the position that material tax liabilities, interest and penalties are payable by us, for example where there has been a technical violation of contradictory laws and regulations that are relatively new and have not been subject to extensive review or interpretation, in which case we expect that we might contest such assessment. High-profile companies can be particularly vulnerable to aggressive application of unclear requirements. Many companies must negotiate their tax bills with tax inspectors who may demand higher taxes than applicable law appears to provide. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

We exercise significant judgment when determining tax filing positions. The tax rules and regulations are very complex and there can be no assurance that management's interpretation and application of these rules and regulations to determine tax filing positions will be accepted by the tax authorities. If the tax authorities reject a tax filing position taken by the Company, it could have a material adverse effect on our financial position and operating results. There is a risk that the tax authorities could impose additional taxable income or disallow the deductibility of expenses on intercompany transactions resulting in higher tax obligations in one or more tax jurisdictions. Management's experience has been that the tax authorities can be aggressive in taking positions that would increase taxable income and/or disallow deductible expenses. If the tax authorities are successful in increasing taxable income and/or disallowing deductible expenses in one or more jurisdictions, it could result in the Company experiencing a higher effective tax rate that could be material. Management regularly consults with professional tax advisors when establishing tax filing positions and believes that the tax filing positions taken are in accordance with tax regulations; however, there is always a risk that the tax authorities could disagree with the tax filing positions taken resulting in additional taxes, interest and penalty becoming due and such amounts could be material.

We may be unable to use tax losses and tax credit carry-forwards and certain built-in losses to reduce future tax payments or benefit from favorable Irish tax legislation.

As an Irish incorporated and tax resident company, we are subject to Irish corporate taxation on our worldwide profits. Due to the nature of our business, we have generated losses since inception and therefore have not paid any Irish corporation tax. As of December 31, 2025, we had unused tax losses of $179.7 million. Subject to any relevant utilization criteria and restrictions (including those that can restrict the use of carried forward losses where there is a change of ownership of more than half of our ordinary shares and a major change in the nature, conduct or scale of the trade) and subject to the related expenses giving rise to the losses being tax deductible, we expect these to be eligible for carry-forward and utilization against future operating profits.

As a company that carries out extensive research and development activities, we seek to benefit from the Irish research and development tax credit for certain expenditure on research and development activities, plant and machinery and buildings as set out in the Taxes Consolidation Act 1997 of Ireland and the Taxes Consolidation Act 1997 (Prescribed Research and Development Activities Regulations) 2004. Credit is given at 25% of allowable expenditure for accounting periods ending on or before December 31, 2023, 30% of allowable expenditure for accounting periods commencing after January 1, 2024, and 35% of allowable expenditure for accounting periods commencing after January 1, 2026, subject to satisfying the applicable conditions.

We may benefit from Ireland's Knowledge Development Box regime in the future. The Irish Finance Act 2022 amended the regime, such that an eligible company is entitled to a corporate tax deduction equal to 20% of its qualifying profits. Qualifying profits are profits directly attributable to the exploitation of certain types of intellectual property (patents, copyrighted computer software) that have been developed by the Irish company through qualifying research and development, or R&D, activities undertaken by the Irish company. In effect, such qualifying profits would be taxed at 10% where the conditions of the regime are met. The availability of the relief is fact dependent and we will consider the applicability of this relief as our activities progress.

When taken in combination with the research and development tax credit, we expect a long-term rate of Irish corporation tax lower than the statutory rate to apply to us. If, however, there are unexpected adverse changes to the Irish research and development tax credit regime or the Knowledge Development Box regime, or for any reason we are unable to qualify for such regimes, or we are unable to use tax losses and tax credit carry-forwards and certain built-in losses to reduce future tax payments then our business, results of operations and financial condition may be adversely affected. This may impact our ongoing requirement for investment and the timeframes within which additional investment is required.

We may become subject to U.S. federal and state forfeiture laws which could negatively impact our business operations.

Violations of any U.S. federal laws and regulations could result in significant fines, penalties, administrative sanctions, convictions or settlements arising from civil proceedings conducted by either the federal government or private citizens, or criminal charges, including, but not limited to, seizure of assets, disgorgement of profits, cessation of business activities or divestiture. As an entity that conducts business involving mebufotenin, we are potentially subject to federal and state forfeiture laws (criminal and civil) that permit the government to seize the proceeds of criminal activity. Civil forfeiture laws could provide an alternative for the federal government or any state (or local police force) that wants to discourage residents from conducting transactions with mebufotenin-related businesses but believes criminal liability is too difficult to prove beyond a reasonable doubt. Also, an individual can be required to forfeit property considered to be the proceeds of a crime even if the individual is not convicted of the crime, and the standard of proof in a civil forfeiture matter is lower than the standard in a criminal matter. Depending on the applicable law, whether federal or state, rather than having to establish liability beyond a reasonable doubt, the federal government or the state, as applicable, may only be required to prove that the money or property at issue is proceeds of a crime by either clear and convincing evidence or a mere preponderance of the evidence.

Investors located in jurisdictions where mebufotenin remains illegal may be at risk of prosecution under conspiracy, aiding and abetting, and money laundering statutes, and be at further risk of losing their investments or proceeds under forfeiture statutes. Many jurisdictions remain fully able to take action to prevent the proceeds of mebufotenin businesses from entering their state. Our investors and prospective investors should be aware of these potentially relevant laws in considering whether to invest in us.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, be precluded from manufacturing GH001 and GH002 and developing and selling GH001, GH002 or any other product candidates outside the United States or be required to develop and implement costly compliance programs, which could adversely affect our business, results of operations and financial condition. Our directors and managers might also be subject to criminal penalties, including jail time.

Our operations are subject to anti-corruption laws, including the Criminal Justice (Corruption Offences) Act 2018 of Ireland, or Criminal Justice Act, the U.S. Foreign Corrupt Practices Act, or FCPA and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Criminal Justice Act, FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage.

The Criminal Justice Act, the FCPA and these other laws generally prohibit us and our employees and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, a financial or other advantage to government officials or other persons to induce them to improperly perform a relevant function or activity (or reward them for such behavior).

Under the Criminal Justice Act, for example, we may also be liable for failing to prevent a person associated with us from committing a bribery offense. We, along with those acting on our behalf and our commercial partners, operate in a number of jurisdictions that pose a high risk of potential Criminal Justice Act or FCPA violations, and we participate in collaborations and relationships with third parties whose corrupt or illegal activities could potentially subject us to liability under the Criminal Justice Act, FCPA or local anti-corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

Compliance with the FCPA in particular, is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

In the future, we may operate in jurisdictions that pose a high risk of potential Criminal Justice Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Criminal Justice Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted. If we expand our operations, we will need to dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the federal government of the United States and authorities in member states of the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations (collectively referred to herein as the Trade Control laws). In addition, various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our international presence, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from manufacturing GH001 or GH002 and developing and selling GH001, GH002 or any other product candidates outside of the United States, and the EU, which could limit our growth potential and increase our development costs.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Criminal Justice Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Criminal Justice Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which would have an adverse impact on our business, financial condition, results of operations and liquidity. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Any investigation of any potential violations of the Criminal Justice Act, the FCPA, other anti-corruption laws or Trade Control laws by Irish, U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Our relationships with healthcare providers and physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Although we do not currently have any products on the market, upon commercialization of our product candidates, if approved, we will be subject to additional healthcare statutory and regulatory requirements and oversight by federal and state governments in the United States as well as foreign governments in the jurisdictions in which we conduct our business. Healthcare providers and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, third-party payors, customers and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business or financial arrangements.

The applicable federal, state and foreign healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the federal Anti-Kickback Statute is violated. Violations are subject to significant civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment and exclusion from government healthcare programs. In addition, a claim submitted for payment to any federal healthcare program that includes items or services that were made as a result of a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims act, or the FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but they are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor;

- the federal civil and criminal false claims laws, including the FCA, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false, fictitious or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs; knowingly making, using or causing to be made or used, a false record or statement material to a false, fictitious or fraudulent claim or an obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. A claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the FCA. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring qui tam actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery or settlement. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA fraud provisions without actual knowledge of the statute or specific intent to violate it;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose, among other things, certain requirements relating to the privacy, security and transmission of individually identifiable health information on certain covered healthcare providers, health plans and healthcare clearinghouses, known as covered entities, as well as their respective "business associates," those independent contractors or agents of covered entities that create, receive, maintain, transmit or obtain protected health information in connection with providing a service on behalf of a covered entity as well as their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

- the federal Physician Payments Sunshine Act, created under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to direct or indirect payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician providers, including physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives, and teaching hospitals, as well as ownership and investment interests held by the physicians and their immediate family members;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- analogous U.S. state, local and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and other relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state and local laws that require the registration of biopharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health and other personal information, some of which may be more stringent than those in the United States (such as the EU's General Data Protection Regulation (Regulation (EU) 2016/679), or GDPR, which became effective in May 2018) in certain circumstances, and may differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The distribution of biopharmaceutical products is subject to additional requirements and regulations, including extensive record keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of biopharmaceutical products.

If the FDA, EMA or a comparable foreign regulatory authority approves any of our product candidates, we will be subject to an expanded number of these laws and regulations and will need to expend resources to develop and implement policies and processes to promote ongoing compliance. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

It is possible that governmental and enforcement authorities will conclude that our business practices, including our arrangements with physicians and other healthcare providers, some of whom may receive share options as compensation for services provided, may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to significant sanctions, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, reputational harm, exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restricting of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to similar penalties. Any action for violation of these laws, even if successfully defended, could cause us to incur significant legal expenses and divert management's attention from the operation of the business. In addition, the approval and commercialization of any product candidate we develop outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws. All of these could harm our ability to operate our business and our financial results.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

Our actual or perceived failure to comply with applicable health information and data protection laws and regulations, standards and other requirements could lead to governmental enforcement actions, including civil or criminal penalties, private litigation, and adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to U.S. and foreign federal, state and local laws and regulations that address privacy and data security. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health and personal information privacy laws, and federal and state consumer protection laws, govern the collection, use, processing, storage, transmission, disclosure, destruction and protection of health-related and other personal information. In addition, we may obtain health information from third parties, including research institutions from which we obtain clinical trial data, which are subject to privacy and security requirements under HIPAA, as amended by HITECH. To the extent that we act as a business associate we may also be subject to the privacy and security provisions of HIPAA, as amended by HITECH, which restricts the use and disclosure of patient-identifiable health information, mandates the adoption of certain standards relating to the privacy and security of patient-identifiable health information, and requires the reporting of certain security breaches to healthcare provider customers with respect to such information. Additionally, many states have enacted similar laws that may impose more stringent requirements on entities like ours. Depending on the facts and circumstances, we could be subject to significant civil, criminal, and administrative penalties if we obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Additionally, in June 2018, the State of California enacted the California Consumer Privacy Act of 2018, or CCPA, which came into effect on January 1, 2020, and provides new data privacy rights for California consumers (as that term is defined in the legislation) and new operational requirements for companies that process information of California residents, which may increase our compliance costs and potential liability. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action and statutory damages for data breaches that is expected to increase data breach litigation. While there is currently an exception under the CCPA for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may nevertheless impact certain of our business activities depending on how the CCPA will be interpreted, and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal information. In addition, the California Privacy Rights Act of 2020, or CPRA, which went into effect on January 1, 2023, imposes additional obligations on companies covered by the legislation and significantly modifies the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also created a new state agency that is vested with authority to implement and enforce the CCPA and CPRA. Other states and the U.S. federal government are considering comprehensive privacy laws. For example, the Virginia Consumer Data Protection Act, which became effective on January 1, 2023, contains provisions that require businesses subject to the legislation to conduct data protection assessments in certain circumstances and that require opt-in consent from Virginia consumers to process certain sensitive personal information. In addition, Colorado enacted the Colorado Privacy Act, and Connecticut enacted the Connecticut Data Privacy Act, each of which took effect on July 1, 2023, and Utah enacted the Consumer Privacy Act, which became effective on December 31, 2023. Several other states, including New Hampshire, Delaware, Nebraska, Nevada and Oklahoma, have also enacted privacy-related laws that have recently gone into effect. Moreover, all 50 states have laws that require the provision of notification for breaches of personal information to affected individuals, state officers or others. These state laws and such other proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies.

The collection, use, storage, disclosure, transfer, or other processing of personal data (including health data processed in the context of clinical trials) regarding EU data subjects in the EEA and/or carried out in the context of our establishment in any EEA member state, is subject to the GDPR, and any legislation which amends, extends, consolidates, re-enacts or replaces the GDPR from time to time.

The GDPR is wide-ranging in scope and imposes numerous additional requirements on companies that process personal data of individuals residing in Europe, including imposing special requirements in respect of the processing of health and other sensitive data, requiring that consent of individuals to whom the personal data relates is obtained in certain circumstances, requiring additional disclosures to individuals regarding data processing activities, requiring that appropriate safeguards are implemented to protect the security and confidentiality of personal data, creating mandatory data breach notification requirements in certain circumstances, and requiring that certain measures (including contractual requirements) are put in place when engaging third-party data processors. The GDPR permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to EUR 20 million or 4% of annual global revenue, whichever is greater. The GDPR also provides individuals with various rights in respect of their personal data, including rights of access, erasure, portability, rectification, restriction and objection, and confer a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. The GDPR requirements apply not only to third-party transactions, but also to transfers of information between us and our subsidiaries, including employee information.

The GDPR and the Irish Data Protection Act 2018 also impose strict rules on the transfer of personal data to countries outside the EEA, including the United States, unless the parties to the transfer have implemented safeguards to protect the transferred personal information. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA to the United States in compliance with law, such as the EEA's standard contractual clauses, and the EU-U.S. Data Privacy Framework, or the Framework (which allows for transfers to U.S.-based organizations that self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges or may be challenged in future, and there is no guarantee that we can satisfy or rely on these measures to lawfully transfer personal data to the United States or other jurisdictions. If there is no lawful manner for us to transfer personal data from the EEA or other jurisdictions to the United States, or if the requirements for a legally compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants and civil society and privacy advocacy groups.

In addition, Europe and other foreign jurisdictions have enacted laws, regulations, standards and common practices that relate to the privacy of clinical trial data, including as a condition to approve clinical trials. These requirements are evolving and uncertain and they may result in delays to our ability to launch clinical trials or limit the jurisdictions in which we may conduct clinical trials.

The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR. While we have taken steps to comply with the GDPR and implementing legislation in applicable EEA member states, including by seeking to establish appropriate lawful bases for the various processing activities we carry out as a controller or joint controller, reviewing our security procedures and those of our vendors and collaborators, and entering into data processing agreements with relevant vendors and collaborators, we cannot be certain that our efforts to achieve and remain in compliance have been, and/or will continue to be, fully successful.

The regulatory framework for data privacy and security issues in the United States and abroad is rapidly evolving and likely to remain uncertain for the foreseeable future. Compliance with applicable privacy and data protection laws and regulations is a rigorous and time-intensive process and could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose certain data, or in some cases, impact our ability to operate in certain jurisdictions. Despite our efforts to bring our practices into compliance with these laws and regulations, we may not be successful in our efforts to achieve compliance due to internal or external factors, such as resource allocation limitations or a lack of vendor cooperation. In addition, because the interpretation and application of privacy and data protection laws are still uncertain, it is possible that these laws and other actual or alleged legal obligations, such as contractual or self-regulatory obligations, may be interpreted and applied in a manner inconsistent with our data management practices. Our failure or perceived failure to comply with these laws, regulations and obligations could result in government investigations, proceedings and enforcement actions (which could include civil, criminal and administrative penalties), public statements against us by government entities, private parties, consumer advocacy groups or others, private litigation, contractual penalties, monetary damages and/or adverse publicity, and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Changes in U.S. and foreign regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; (iv) additional record keeping requirements; or (v) discounts or other price reductions on our products. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States and in some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative initiatives and regulatory changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the ACA was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. biopharmaceutical industry.

While there have been numerous judicial, administrative, executive and legislative challenges to certain aspects of the ACA, the ACA remains in effect. It is possible that the ACA will be subject to additional challenges. It is unclear how any such challenges will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011 imposed, subject to certain temporary suspension periods, 2% reductions in Medicare payments to providers per fiscal year starting April 1, 2013, and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, unless additional Congressional action is taken. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs was eliminated. Elimination of this cap has, in some cases, required pharmaceutical manufacturers to pay more in rebates than they received on the sale of products.

There has been heightened governmental scrutiny over the manner in which manufacturers set prices for their products, which has resulted in several presidential executive orders, Congressional inquiries, and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare, and reform government program reimbursement methodologies for drug products. For example, several healthcare reform initiatives culminated in the enactment of the Inflation Reduction Act, or the IRA, in August 2022, which, among other things, requires HHS to directly negotiate the selling price of a statutorily specified number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. The negotiated price may not exceed a statutory ceiling price. Only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for single-source biologics) are eligible to be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. For 2026, the first year in which negotiated prices become effective, CMS selected 10 high-cost Medicare Part D products in 2023, negotiations began in 2024, and the negotiated maximum fair price for each such product has been announced. In addition, CMS has selected and announced the negotiated maximum fair price for 15 additional Medicare Part D drugs, which will become effective in 2027. For 2028, CMS selected an additional 15 drugs, comprised of drugs covered under Medicare Part D and, for the first time, drugs payable under Medicare Part B. For 2029 and subsequent years, 20 Part B or Part D drugs will be selected. Currently, a drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA's price negotiation requirements, but will lose that exclusion if it has designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. However, as a result of a statutory amendment enacted in July 2025, beginning with the 2028 negotiated price applicability year, a drug may be designated for more than one rare disease or condition and still be excluded from price negotiation, as long as the only approved indications are for such rare diseases or conditions. The IRA also imposes rebates on Medicare Part D and Part B drugs whose prices have increased at a rate greater than the rate of inflation, and in November 2024, CMS finalized regulations for the Medicare Part B and Part D inflation rebates. The IRA also eliminated, beginning in 2025, the coverage gap under Medicare Part D by significantly lowering the enrollee maximum out-of-pocket cost and requiring manufacturers, in order for their drugs to be reimbursed by Medicare Part D, to subsidize, through a newly established manufacturer discount program, 10% of Part D enrollees' prescription costs for brand drugs below the out-of-pocket limit, and 20% once the out-of-pocket limit has been reached. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, some significant, including civil monetary penalties. These provisions may be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers. Thus, while it is unclear how the IRA will be implemented, it will likely have a significant impact on the biopharmaceutical industry and the pricing of our products and product candidates.

In addition, in May 2025, the administration published an executive order regarding most favored nation, or MFN, drug pricing, which is sometimes referred to as international reference pricing. This executive order directs the Secretary of HHS to communicate MFN price targets to pharmaceutical manufacturers, and if significant progress towards MFN pricing is not delivered, to propose a rulemaking plan to implement MFN pricing. Recently, on December 23, 2025, CMS issued proposed regulations to establish, under the Center for Medicare and Medicaid Innovation, two mandatory MFN demonstration models under Medicare Parts B and D, respectively. If these rules or other MFN pricing rules are finalized, they are likely to mandate reduced prices of at least some drugs in the United States, if they are also sold in comparator countries.

At the state level in the United States, legislatures are increasingly enacting laws and implementing regulations designed to control pharmaceutical and biologic product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, the FDA released a final rule in September 2020 providing guidance for states to build and submit importation plans for certain prescription drugs from Canada into the United States, and the FDA authorized the first such plan in Florida in January 2024. This plan has been granted extensions until May 6, 2026. It is unclear how this program will be implemented, if at all, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada.

Legally mandated price controls on payment amounts by third-party payors or other restrictions on coverage or access could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates that we successfully commercialize or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidate, restrict or regulate post-approval activities and affect our ability to commercialize any products for which we obtain marketing approval. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In April 2023, the European Commission proposed a legislative package to revise EU pharmaceutical legislation. This proposal, which comprises a directive and regulation, has received provisional political agreement between the European Commission, the European Parliament and the Council of the EU, but remains subject to formal adoption by the European Parliament and the Council of the EU.

Legislation changes may also affect the legal requirements under which we perform our technical, nonclinical and clinical development of our product candidates and the medical devices required to deliver such product candidates, and they may affect how the FDA, EMA and comparable foreign regulatory agencies review and approve new drug products, drug-device combination products or medical devices. For example, on April 5, 2017, the European Parliament passed the MDR, which repeals and replaces the EU Medical Devices Directive and the Active Implantable Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the EEA member states, regulations are directly applicable, i.e., without the need for adoption of EEA member state laws implementing them, in all EEA member states and are intended to eliminate current differences in the regulation of medical devices among EEA member states. The MDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EEA for medical devices and ensure a high level of safety and health while supporting innovation.

The MDR became fully applicable on May 26, 2021, after a three-year transition period. This regulation, among other things:

- strengthens the rules on placing medical devices on the market and reinforces surveillance once they are available;
- establishes explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance and safety of medical devices placed on the market;
- improves the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number;
- sets up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the EU; and
- strengthens rules for the assessment of certain high-risk medical devices, such as implants, which may have to undergo an additional check by experts before they are placed on the market.

These modifications may have a significant effect on the way we can develop our product candidates and the medical devices required to deliver such product candidates, and may delay our development significantly.

On March 20, 2023, Regulation (EU) 2023/607 entered into force, which extended the transitional provisions of the MDR as follows:

- 2026 for class III custom made devices;
- 2027 for class III and class IIb implantable devices;
- 2028 for other class IIb, class IIa and class Is, Im devices; and
- 2028 for class I up classified devices.

The transitional provisions allow time for devices CE marked under the Directives to transition and become CE marked under the MDR.

In addition, the EU adopted the Clinical Trials Regulation, or Regulation 536/2014, or CTR, in April 2014, which became applicable on January 31, 2022. The CTR is directly applicable in all the EU member states, and repeals the Clinical Trials Directive. The CTR contained a transitional timeline, which ended on January 31, 2025, requiring all ongoing clinical trials to have transitioned to the CTR with effect from this date.

The CTR harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which will notably contain a centralized EU portal and database.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or in any other jurisdictions. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

In the United States, inadequate funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes, including changes to the FDA's priorities or processes. The FDA has faced proposed and enacted funding cuts, leading to significant reductions in discretionary funding which has, and may in the future, impact staffing and operations of the FDA. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. See "Risks Related to Our Financial Position and Need for Additional Capital - Failure of the U.S. federal government to manage its fiscal matters or to raise or further suspend the debt ceiling may expose us to increased financial and operational risk."

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. For example, starting in January 2025, the U.S. government has reduced the number of federal employees, including at the FDA, which could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. In addition, over the last several years, and most recently in October 2025, the U.S. federal government has shut down several times and certain regulatory agencies, such as the FDA have had to furlough critical employees and stop critical activities. If a prolonged government shutdown recurs, or if the FDA is otherwise hindered by inadequate funding, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns or similar funding issues could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the EU member states.

We ultimately intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of drugs is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future healthcare reform measures.

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU member states. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in most foreign countries, including those in the EU and the EEA, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected.

If we or any third parties working with mebufotenin whom we engage fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We, and third parties working on our behalf, are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations and the operations of third parties operating on our behalf may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In particular, there is limited toxicology data on mebufotenin, and the risk of contamination and injury is higher as we and third parties working on our behalf work with mebufotenin in its aerosolized form. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain employer's liability insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Risks Related to Intellectual Property

We rely on patents, applications for patents and other intellectual property rights to protect our GH001 and GH002 product candidates, the prosecution, enforcement, defense and maintenance of which may be challenging and costly. Failure to adequately prosecute, maintain, enforce or protect these rights could harm our ability to compete and impair our business.

Our commercial success depends in part on obtaining and maintaining patents and other forms of intellectual property rights relating to GH001, GH002 and any future product candidates, methods used to manufacture the underlying therapeutic substances, compositions and methods for treating patients using those substances and therapies and medical devices used to deliver such substances and therapies, or licensing such rights from third parties. Failure to obtain, maintain, protect, enforce or extend adequate patent and other intellectual property rights could materially adversely affect our ability to develop and market GH001, GH002 and any future product candidates, and medical devices to deliver such product candidates. We also rely on trade secrets and know-how to develop and maintain our proprietary and intellectual property position. Any failure to protect our trade secrets and know-how could similarly adversely affect our operations and prospects.

We cannot be certain that patents will be issued or granted with respect to our or any of our future licensors' pending and future patent applications, or that any of our or our future licensors' issued or granted patents will not later be found to be invalid or unenforceable. The patent position of companies like ours is generally uncertain because it involves complex legal and factual considerations and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights is highly uncertain. The standards applied by the European Patent Office, the United States Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in pharmaceutical patents. Consequently, patents may not issue from our pending patent applications, and even if they do issue, such patents may not issue in a form that effectively prevents others from developing or commercializing competing therapies. As such, we do not know the degree of future protection that we will have on our proprietary therapies. This risk is further heightened with respect to our GH001 and GH002 product candidates given that the molecule mebufotenin is a known naturally occurring substance.

The patent prosecution process is expensive, complex and time-consuming, and we and any of our third-party licensors, licensees, or collaboration partners may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our licensors, licensees or collaboration partners will fail to identify patentable aspects of inventions made in the course of research, development or commercialization activities before it is too late to pursue patent protection on them. In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach these agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not published until and unless granted. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Similarly, we cannot be certain that for any in-licensed patents or pending patent applications, the named applicant(s) would be the first to make the inventions claimed in such patents or pending patent applications or that the named applicant(s) would be the first to file for patent protection for such inventions.

Moreover, in some circumstances, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications covering technology that we license from or license to third parties, and may be reliant on our licensors, licensees or collaboration partners to do so. Therefore, these patents and applications may not be prepared, filed, prosecuted, maintained, enforced or defended in a manner consistent with the best interests of our business. If any of our current or future licensors, licensees or collaboration partners fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If any of our licensors, licensees or collaboration partners are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patents and other intellectual property rights, such rights could be compromised and our right to develop and commercialize our product candidates that are subject to such license rights could be adversely affected.

The patent examination process may also require us or our licensors, licensees or collaboration partners to narrow the scope of the claims of our or our licensors', licensees' or collaboration partners' pending and future patent applications, which may limit the scope of patent protection that may be obtained. We cannot assure you that all of the potentially relevant prior art relating to our or any of our licensors', licensees' or collaboration partners' patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our or any of our licensors', licensees' or collaboration partners' patents may be challenged in the courts or patent offices in the United States and abroad. Even if patents do successfully issue and even if such patents cover GH001, GH002 and any other product candidates, third parties may initiate an opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation proceedings in court or before patent offices, or similar proceedings challenging the validity, enforceability or scope of such patents. For example, various third parties have filed opposition papers challenging our issued EP patents, directed to mebufotenin or a pharmaceutically acceptable salt thereof for use in treating patients diagnosed with MDD and to the crystalline salt mebufotenin HBr. Any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and therapies, or limit the duration of patent protection of our technology and product candidates.

Our and our licensors', licensees' or collaboration partners' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology in the relevant country. In addition, patents and other intellectual property rights will not protect our technology, GH001, GH002 or any other product candidates or medical devices to deliver such product candidates if third parties, including our competitors, design around our protected technology, GH001, GH002 or any other product candidates or medical devices to deliver such product candidates without infringing, misappropriating or otherwise violating our owned or in-licensed patents or other intellectual property rights. Moreover, some of our patents and patent applications may be co-owned with third parties in the future. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing therapies and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Because patent applications are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors, licensees or collaborators were or will be the first to file any patent application related to a product candidate. Furthermore, if U.S. patent applications of third parties have an effective filing date before March 16, 2013, an interference proceeding can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If U.S. patent applications of third parties have an effective filing date on or after March 16, 2013, a derivation proceeding can be initiated by such third parties to determine whether our invention was derived from theirs. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing our invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. In addition, we may be subject to third-party challenges regarding our exclusive ownership of our intellectual property. If a third party were successful in challenging our exclusive ownership of any of our intellectual property, we may lose our right to use such intellectual property, such third party may be able to license such intellectual property to other third parties, including our competitors, and our competitors could market competing therapies and technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, we may develop, acquire or license intellectual property rights that have been generated through the use of U.S. government funding. As a result, the U.S. government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with U.S. government funding, the U.S. government generally obtains certain rights in any resulting patents, including a non-exclusive, worldwide, irrevocable license authorizing the U.S. government to use the inventions for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our technology. The U.S. government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and prospects.

We may be involved in lawsuits or administrative proceedings to protect or enforce our patents or other intellectual property rights, and issued patents covering one or more of our product candidates could be found invalid or unenforceable if challenged in court.

Competitors or other third parties may infringe, misappropriate or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To protect our competitive position, we may from time to time need to resort to litigation in order to enforce or defend any patents or other intellectual property rights owned by or licensed to us, or to determine or challenge the scope or validity of patents or other intellectual property rights of third parties. Enforcement of intellectual property rights is difficult, unpredictable and expensive, and many of our or our licensors' or collaboration partners' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions and better sustain the costs of such actions than we or our licensors or collaboration partners can. Accordingly, despite our or our licensors' or collaboration partners' efforts, we or our licensors or collaboration partners may not prevent third parties from infringing upon, misappropriating or otherwise violating intellectual property rights we own or control, particularly in countries where the laws may not protect those rights as fully as in the EU and the United States. We may also fail in enforcing our rights, in which case our competitors and other third parties may be permitted to use our therapies or other technologies without payment to us.

In addition, litigation involving our patents carries the risk that one or more of our patents will be narrowed, held invalid (in whole or in part, on a claim-by-claim basis) or held unenforceable. Such an adverse court ruling could allow third parties to commercialize our therapies or other technologies, and then compete directly with us, without payment to us.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the European Patent Office, or the USPTO, or made a misleading statement during prosecution. In patent litigation in the United States or in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. A claim for a validity challenge may be based on failure to meet any of several statutory requirements, for example, lack of novelty, obviousness, lack of written description or non-enablement. Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover GH001, GH002 or any other product candidates or medical devices to deliver such product candidates. The outcome following legal assertions of invalidity and unenforceability during patent litigation or other proceedings is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant or third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on GH001, GH002 or one or more of any other product candidates or medical devices to deliver such product candidates. Such a loss of patent protection could have a material adverse impact on our business financial condition, results of operations, and prospects. Further, litigation could result in substantial costs and diversion of management resources, regardless of the outcome, and this could harm our business and financial results.

We may also be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. It is possible that we do not perfect our ownership of all patents, patent applications and other intellectual property. This possibility includes the risk that we do not identify all inventors, or identify incorrect inventors, which may lead to claims disputing inventorship or ownership of our patents, patent applications and other intellectual property by former employees or other third parties. There is also a risk that we do not establish an unbroken chain of title from inventors to us. Errors in inventorship or ownership can sometimes also impact priority claims. If we were to lose the ability to claim priority for certain patent filings, intervening art or other events may preclude us from being issued patents. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to monetary damages, we may lose valuable intellectual property rights. Such an outcome could significantly harm our business and financial results.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance, renewal, annuity and various other governmental fees on any issued or applied-for patents are due to be paid to the European Patent Office, the USPTO and foreign patent agencies in several stages over the lifetime of a patent. The European Patent Office, the USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain circumstances, we may rely on our collaboration partners, law firms or other professionals to pay these fees due to the USPTO and comparable foreign patent agencies and to take the necessary action to comply with such requirements with respect to our intellectual property. While instances of inadvertent non-compliance can, in many cases, be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of a patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our service providers, licensors or collaboration partners fail to maintain the patents and patent applications covering our product candidates, our patent protection could be reduced or eliminated and third parties, including our competitors, might be able to enter the market with similar or identical therapies or technologies, which would have a material adverse effect on our business, financial condition, results of operations, and prospects. In addition, if we fail to apply for or otherwise fail to obtain applicable patent term extensions or adjustments as a result of such non-compliance, we will have a more limited time during which we can enforce our granted patent rights. Further, if we are responsible for patent prosecution and maintenance of patent rights in-licensed to us, any of the foregoing could expose us to liability to the applicable patent owner.

If we do not obtain protection under the Hatch-Waxman Act and similar foreign legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

In the United States, if all maintenance fees are paid on time, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but there can be no assurance that any such extensions will be obtained, and the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates, their manufacture or use are obtained, once the patent life has expired, we may be open to competition from competitive therapies or technologies. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates and concomitant therapies might expire before or shortly after such candidates and concomitant therapies are commercialized. As a result, our owned and in-licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing therapies similar or identical to ours.

Depending upon the timing, duration and conditions of FDA marketing approval of GH001, GH002 and any other future product candidates and medical devices to deliver such product candidates, one or more U.S. patents that we may own or license in the future may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the normal expiration for a patent covering an approved product as compensation for effective patent term loss during product development and the FDA regulatory review process. The patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, is limited to the approved indication (or any additional indications approved during the period of extension) and only one patent per approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method of manufacturing it may be extended. Patent term extension, or other related rights such as supplementary protection certificates, may also be available in certain foreign jurisdictions, including the EU, upon regulatory approval of any product candidates we develop. However, we may not receive an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will not be lengthened and third parties, including our competitors, may obtain approval to market competing therapies sooner than we expect. As a result, our revenue from applicable therapies could be materially reduced and our business, financial condition, results of operations, and prospects could be materially harmed.

Intellectual property rights do not necessarily address all potential threats to our business and competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make compositions that are the same as or similar to GH001, GH002 and any other product candidate compositions, or may be able to make medical devices to deliver such compositions, that are not covered by the claims of the patents that we own or license;
- the patents of third parties may have an adverse effect on our business;
- we or our licensors or collaboration partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patent or pending patent application that we own or license;
- we or our licensors or collaboration partners might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating or otherwise violating our intellectual property rights;
- it is possible that current and future pending patent applications we own or in-license will not lead to issued patents;
- issued patents that we own or in-license may not provide us with any competitive advantage, or may be held invalid or unenforceable as a result of legal challenges by third parties;
- issued patents that we own or in-license may not have sufficient term or geographic scope to provide meaningful protection;
- our competitors might conduct research and development activities in countries that provide a safe harbor from patent infringement claims for certain research and development activities or in countries where we do not have patent rights and then use the information learned from such activities to develop competitive therapies for sale in our major commercial markets;

- third parties performing manufacturing or testing for us using our therapies or technologies could use the intellectual property of others without obtaining a proper license;
- we may not develop additional technologies that are patentable; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property, or otherwise develop similar know-how.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may be subject to claims by third parties asserting that we or our employees, consultants or advisors have misappropriated their intellectual property, including trade secrets, or claiming ownership of what we regard as our own intellectual property.

Many of our consultants, advisors and employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies, including our competitors and potential competitors. Some of these individuals executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we intend that our consultants, advisors and employees do not use proprietary information or know-how of their former employers while working for us, we may be subject to claims that we or these individuals have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such individual's former employer. Litigation may be necessary to defend against these claims, regardless of their merit, and we cannot predict whether we would prevail in any such actions. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages, our development and commercialization efforts may be prevented or delayed, and we could be required to obtain a license from such third party to commercialize our therapies or other technologies. Such a license may not be available on commercially reasonable terms or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract our management from its day-to-day activities, and may cause negative publicity.

In addition, we may be subject to claims by our current or former employees or contractors asserting an ownership right in our intellectual property as a result of the work they performed on our behalf. While it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, for which we may not have an adequate remedy, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Intellectual property rights of third parties could adversely affect our ability to compete or commercialize our product candidates. Third parties may allege that we are infringing, misappropriating or otherwise violating their intellectual property rights such that we could be required to litigate or obtain licenses from third parties in order to develop or market our product candidates, which could be costly and have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability and the ability of our current and future collaborators to develop, manufacture, market, and sell any product candidates and devices to deliver such product candidates that we may develop and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In the future, we may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to GH001, GH002 or any other product candidates or medical devices to deliver such product candidates. If the outcome of any such proceeding or litigation is adverse to us, it may affect our ability to compete effectively.

Additionally, our competitive position may suffer if patents issued to third parties, or other third-party intellectual property rights, cover our therapies or elements thereof, our manufacture or uses relevant to our development plans, the targets of GH001, GH002 or any other product candidates, or medical devices to deliver such product candidates, or other attributes of GH001, GH002 or any other product candidates. In such cases, we may not be in a position to develop or commercialize such product candidates or devices to deliver such product candidates unless we successfully pursue litigation to nullify or invalidate the third-party intellectual property right concerned, or enter into a license agreement with the intellectual property right holder, which may not be available on commercially reasonable terms or at all. In the event that a patent has not expired at the time of approval of such product candidate(s) and the patent owner were to bring an infringement action against us, we may have to argue that our product candidates or the manufacture or use of the underlying therapeutic substances or devices to deliver such product candidates do not infringe a valid claim of the patent in question. Alternatively, if we were to challenge the validity of any issued U.S. patent in court, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that in order to prevail, we would need to present clear and convincing evidence as to the invalidity of the patent's claims. The same applies to certain other jurisdictions. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. In the event that a third party successfully asserts its patent against us such that such third party's patent is found to be valid and enforceable and infringed by our product candidates, unless we obtain a license to such patent, under which we would most likely be required to pay various types of fees, milestones, royalties or other amounts, and which may not be available on commercially reasonable terms or at all, we could be prevented from continuing to develop or commercialize our product candidates without an effective redesign, which may not be feasible from a technical perspective, or in a timely manner from a commercial perspective, either of which could have a material adverse effect on our business.

It is possible that we have failed, and in the future may fail, to identify relevant patents or applications that may be asserted against us. For example, certain U.S. patent applications filed after November 29, 2000, can remain confidential until and unless issued as patents, provided that inventions disclosed in the applications have not and will not be the subject of a corresponding application filed outside the United States. In general, patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our therapies could have been filed by others without our knowledge. Furthermore, we operate in a highly competitive field, and given our limited resources, it is unreasonable to monitor all patent applications in the areas in which we are active. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our therapies or the use of our therapies.

Third-party intellectual property right holders, including our competitors, may actively bring infringement, misappropriation or violation claims against us based on existing or future intellectual property rights, regardless of their merit. We may not be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage or continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing our therapies. Moreover, we may face patent infringement claims from nonpracticing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect.

If we are unsuccessful in defending any such claim, in addition to being forced to pay damages, we or our licensees may be temporarily or permanently prohibited from commercializing any of our product candidates or devices to deliver such product candidates that were held to be infringing. If possible, we might be forced to redesign GH001, GH002 or any other product candidates or medical devices to deliver such product candidates so that we no longer infringe the intellectual property rights of third parties, or we may be required to seek a license to any such technology that we are found to infringe, which license may not be available on commercially reasonable terms or at all. Even if we or our licensors or collaboration partners obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors or collaboration partners and it could require us to make significant licensing and royalty payments. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. We could also be required to indemnify collaborators or contractors against such claims. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

In addition, if the breadth or strength of protection provided by our or our licensors' or collaboration partners' patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Intellectual property litigation could cause us to spend substantial resources, distract our personnel from their normal responsibilities, harming our reputation and our business operations.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs or in-license needed technology. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development and commercialization activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property proceedings could have a material adverse effect on our ability to compete in the marketplace.

We may not be successful in obtaining or maintaining necessary rights to GH001, GH002 or any other product candidates or any medical devices to deliver such product candidates through acquisitions and in-licenses.

In the future, our programs may require the use of intellectual property or proprietary rights held by third parties, and the growth of our business will likely depend in part on our ability to acquire, in-license, maintain and use these intellectual property and proprietary rights.

For our GH001 inhaled product candidate, for current and previous clinical trials, we acquire the device used to create the inhaled aerosol from a third party. The device and our uses thereof may be covered by one or more patents issued to such third party or other third parties, or other intellectual property rights of such third party or other third parties. We do not currently have a commercial supply agreement with this third party, nor have we established license agreements with any alternative provider of a suitable device. In 2021, we initiated the development of a proprietary aerosol delivery device for GH001 for use in our pivotal clinical trial program and for commercial use. However, despite our efforts to proactively identify any such third-party rights, this proprietary device and our uses thereof may be covered by one or more patents issued to third parties, or other intellectual property rights of third parties. In the event that a third party successfully asserts its intellectual property rights against us, unless we obtain a license to such intellectual property rights, under which we would most likely be required to pay various types of fees, milestones, royalties or other amounts, and which may not be available on commercially reasonable terms or at all, we could be prevented from continuing to develop or commercialize our proprietary aerosol delivery device for GH001. Further, for GH002 and any future delivery platforms that include the use of a device, we plan to either license or acquire the required delivery devices from third parties or work with a CDMO to develop such device and establish manufacturing capabilities for such device. However, we may not be able to in-license the relevant technology, acquire the required delivery device or develop a proprietary delivery device, and our competitive position may suffer if we are unable to obtain necessary commercial supply agreements, licenses, or development agreements with the third parties.

In addition, with respect to any patents we may co-own with third parties, we may require licenses to such co-owners' interest in such patents.

We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for GH001, GH002 or any other product candidates or medical devices to deliver such product candidates on commercially reasonable terms or at all. For example, we may collaborate with U.S. and foreign academic institutions to accelerate our nonclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our applicable investigational therapy or program.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. If we are unable to successfully acquire or obtain a license to third-party intellectual property rights necessary for the development of an investigational therapy or program, or maintain the existing intellectual property rights we have, we may have to abandon development of that investigational therapy or program, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Furthermore, even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general or prevent us from obtaining adequate patent protection, and thereby impair our ability to protect our product candidates.

As is the case with other companies in our industry, our success is heavily dependent on obtaining, maintaining, protecting and enforcing our intellectual property rights, particularly patents. Obtaining and enforcing patent rights in the pharmaceutical industry involves technological and legal complexity, and is costly, time-consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States or other jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. For example, the America Invents Act, or the AIA, enacted in the United States in 2012 and 2013, has resulted in significant changes to the U.S. patent system.

Prior to the enactment of the AIA, assuming that other requirements for patentability are met, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 16, 2013, under the AIA, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention regardless of whether a third party was the first to invent the claimed invention. Under this regime, a third party that files a patent application in the USPTO before us could be awarded a patent covering an invention of ours even if we made the invention before the third party. The AIA requires us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other significant changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and provide additional opportunities for third parties to challenge any pending patent application or issued patent in the USPTO. Such opportunities include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter partes review and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim in any of our future U.S. patents invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use USPTO procedures to invalidate patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of any of our future U.S. patent applications and the enforcement or defense of any patents that may issue from such patent applications.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we might obtain in the future. In particular, Europe's new Unified Patent Court, or UPC, may give rise to uncertainties relating to our ability to enforce our existing patent applications and any patents that we might obtain in the future. This new court came into force on June 1, 2023, and while it is intended to bring significant benefits to patent holders, including greater efficiency and certainty to patent enforcement in the UPC signatory states, it also provides parties with a new means by which to centrally revoke European patents in the countries over which it has jurisdiction, which may change over time. As it is a newly established court, the full scope of patent rights and remedies that will be afforded to patentees under the UPC will not become clear for a number of years. We will have the ability to opt our patents out of this system for the first seven years of the UPC's existence but doing so might preclude us from availing of the advantages this jurisdiction has to offer.

If we fail to comply with our obligations under the agreements pursuant to which we license intellectual property rights to or from third parties, or otherwise experience disruptions to our business relationships with our licensors, licensees or collaborators, we could lose the rights to intellectual property that is important to our business and lose the ability to continue the development and/or commercialization of our product candidates.

We are party to development agreements with CDMOs under which we grant such CDMOs non-exclusive rights to use certain of our intellectual property as necessary for such CDMOs to perform their obligations under such agreements, and under which we are granted non-exclusive rights to use certain of such CDMOs' intellectual property as necessary in order to use and exploit such CDMOs' deliverables under such agreements. We expect that we may need to enter into additional license or collaboration agreements in the future that may be important to our business. We expect that future license agreements may impose various financial and other obligations on us related to, among other things, therapeutic development and payment of royalties and fees based on achieving certain milestones. In addition, under such future license agreements, we may be prohibited from developing and commercializing therapies that would compete with the therapies licensed under such agreements. If we fail to comply with our obligations under these agreements, our licensor or collaboration partner may have the right to terminate the agreement, including any licenses included in such agreement, and we may face other liabilities for breach of such agreement.

The termination of any license or collaboration agreements or failure to adequately protect our or our collaborators' rights under such license or collaboration agreements could prevent us from further developing or commercializing GH001, GH002 or any other product candidates or medical devices to deliver such product candidates covered by the agreement or intellectual property licensed thereunder. For example, we may rely on license agreements which grant us rights to certain intellectual property and proprietary materials that we use in connection with the development of our therapies. If such agreements were to terminate, we may be unable to timely license similar intellectual property and proprietary materials from an alternate source, on commercially reasonable terms or at all, and may be required to conduct additional bridging studies on GH001, GH002 or any other product candidates or medical devices to deliver such product candidates or redesign our product candidates, or medical devices, or the methods for manufacturing them, which could delay or otherwise have a material adverse effect on the development and commercialization of GH001, GH002 or any other product candidates or medical devices to deliver such product candidates.

Our existing and future license agreements may also contain sublicenses from third parties which are not the original licensor of the intellectual property at issue. Under these agreements, we must rely on our licensor to comply with its obligations under the primary license agreements under which such third party obtained rights in the applicable intellectual property, where we may have no relationship with the original licensor of such rights. If our licensors fail to comply with their obligations under these upstream license agreements, the original third-party licensor may have the right to terminate the original license, which may terminate the sublicense. If this were to occur, we would no longer have rights to the applicable intellectual property and, in the case of a sublicense, if we were not able to secure our own direct license with the owner of the relevant rights, which we may not be able to do at a reasonable cost or on reasonable terms, it may adversely affect our ability to continue to develop and commercialize GH001, GH002 or any other product candidates or medical devices to deliver such product candidates incorporating the relevant intellectual property.

Disputes may arise regarding intellectual property subject to a license or collaboration agreement, including the following:

- the scope of rights granted under the agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property of the licensor or collaboration partner that is not subject to the agreement;
- the sublicensing of patents and other rights under any current or future collaboration relationships;
- our diligence obligations under the agreement and what activities satisfy those diligence obligations;
- our rights to transfer or assign the agreement;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaboration partners; and
- the priority of invention of patented technology.

In addition, third-party license and collaboration agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidate, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

Obligations, including contractual relationships with and statutory requirements regarding employees and others may not adequately prevent disclosure of our trade secrets and protect other proprietary information.

We consider our trade secrets and proprietary confidential and unpatented know-how to be important to our business. We rely on trade secrets and confidential know-how to protect our proprietary technology, especially where patent protection is believed to be of limited value. However, trade secrets and know-how are difficult to maintain as confidential and we may, at times, have to share our trade secrets and confidential know-how with third parties with whom we collaborate for development, manufacturing or commercialization (e.g. via joint research and development programs), or with regulatory agencies with whom we interact during development and to secure approval of our current or future product candidates.

To protect this type of information against disclosure or misappropriation by third parties and our competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements with us. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or confidential know-how. Also, current or former employees, consultants, contractors and advisors may unintentionally or willfully disclose our trade secrets and confidential know-how to our competitors and other third parties or breach such agreements. We rely on the statutory and regulatory confidentiality obligations certain regulatory agencies have to us when submitting information to them. These obligations may not be adequate to protect our trade secrets and confidential know-how from disclosure and unauthorized use. Monitoring unauthorized uses and disclosures is difficult, and enforcing a claim that a third party illegally obtained and is using our trade secrets or confidential know-how is difficult, expensive, time-consuming and unpredictable. The enforceability of confidentiality obligations may vary from jurisdiction to jurisdiction and courts outside the United States are sometimes less willing to protect trade secrets. We may not be able to obtain an adequate remedy for such disclosures either because it was not awarded to us or if it is unavailable under the local laws and jurisprudence. Furthermore, if a competitor or other third party lawfully obtained or independently developed any of our trade secrets or confidential know-how, we would have no right to prevent such competitor or other third party from using that technology or information to compete with us, which could harm our competitive position. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating such trade secrets. If any of our trade secrets were to be disclosed to, or independently developed by a competitor or other third party, or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be materially and adversely harmed.

Failure to obtain or maintain trade secret protection could adversely affect our competitive position. Moreover, our competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, our competitors could limit our use of our trade secrets or confidential know-how.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We expect to rely on trademarks in the future as a means to distinguish our product candidates that are approved for marketing from the products of our competitors. We have not yet selected trademarks for our product candidates and have not yet begun the process of applying to register trademarks for GH001, GH002 or any other product candidates. Once we select trademarks and apply to register them, our trademark applications may not be approved. Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks, in which case we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Accordingly, we may not be able to adequately protect our rights to these trademarks and trade names, which we need to build name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. If other entities use trademarks similar to ours in different jurisdictions, or have senior rights to ours, it could interfere with our use of our trademarks throughout the world.

We may not be able to protect our intellectual property rights throughout the world and may face difficulties in certain jurisdictions, which may diminish the value of intellectual property rights in those jurisdictions and negatively impact our business.

We or our licensors have not pursued or maintained, and may not pursue or maintain in the future, patent protection for our product candidates in every country or territory in which we may sell our products, if approved. Filing, prosecuting and defending patents covering product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive and our licensors' or collaboration partners' intellectual property rights in some countries outside of, for instance, the member states of the European Patent Convention and the United States, could be less extensive than those in the member states of the European Patent Convention and the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries, or from selling therapies or importing therapeutic compositions made using our inventions in and into, for instance, the member states of the European Patent Convention and the United States, or other jurisdictions. In addition, we may decide to abandon national and regional patent applications before grant. Furthermore, the grant proceeding of each national/regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant patent offices, while granted by others. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

Competitors may use our and our licensors' or collaboration partners' technologies in jurisdictions where we have not obtained patent protection to develop their own therapies and, further, may export otherwise infringing therapies to territories where we and our licensors or collaboration partners have patent protection, but where enforcement is not as strong as in other jurisdictions. These therapies may compete with GH001, GH002 or any other product candidates, and our and our licensors' or collaboration partners' patents or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in, for instance, the member states of the European Patent Convention and the United States, and companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions.

Some countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors or collaboration partners is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired and our business and results of operations may be adversely affected.

Proceedings to enforce our and our licensors' or collaboration partners' patent rights in foreign jurisdictions could result in substantial costs and divert our and our licensors' or collaboration partners' efforts and attention from other aspects of our business, regardless of whether we or our licensors or collaboration partners are successful, and could put our and our licensors' or collaboration partners' patents at risk of being invalidated or interpreted narrowly. In addition, such proceedings could put our and our licensors' or collaboration partners' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors or collaboration partners. We or our licensors or collaboration partners may not prevail in any lawsuits that we or our licensors or collaboration partners initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Our Dependence on Third Parties

We rely on third parties to assist in conducting our nonclinical studies and clinical trials. If they do not perform satisfactorily, we may not be able to initiate new clinical trials, successfully complete clinical trials, obtain regulatory approval or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, such as laboratories, CROs, clinical data management organizations, medical institutions, clinical investigators and consultants, to organize, support or conduct our nonclinical studies and clinical trials and expect to rely on these third parties to conduct nonclinical studies and clinical trials of any other product candidate that we develop. Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Although our reliance on these third parties for nonclinical and clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our nonclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. Moreover, human clinical research must comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and IRBs. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the regulatory authorities may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, a regulatory authority will determine that any of our clinical trials comply with GCPs.

The third parties conducting nonclinical studies and clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These outside contractors may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

If our relationships with any third parties conducting our studies are terminated, we may be unable to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. Switching or adding third parties to conduct our studies involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired nonclinical and clinical development timelines. Although we carefully manage our relationships with third parties conducting our studies, we cannot assure that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material and adverse effect on our business, financial condition and results of operations.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or regulatory approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

The development and manufacture of our active pharmaceutical ingredients, product candidates and medical devices required to deliver such product candidates is complex, and we may encounter difficulties during further development or in production. We currently rely completely on third parties to develop, formulate and manufacture our nonclinical study and clinical trial supplies. The development and commercialization of any of our active pharmaceutical ingredients, product candidates and medical devices required to deliver such product candidates could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of such drug supplies or fail to do so at acceptable quality levels, including in accordance with rigorously enforced regulatory requirements or contractual obligations, and our operations could be harmed as a result.

The processes involved in developing and manufacturing our drug substance, product candidates and medical devices required to deliver such product candidates are complex, expensive, highly regulated and subject to multiple risks. Further, as drug substance, product candidates and medical devices required to deliver such product candidates are developed through nonclinical studies, from early-stage clinical trials to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the drug substance, product candidates and medical devices required to deliver such product candidates, such as technical specifications, design, features and manufacturing methods, are altered along the way in an effort to optimize performance, processes and results and to fulfill regulatory requirements, which are stricter for late-stage clinical trials and commercial manufacture than for early-stage trials. We are currently implementing such changes, which carries the risk that they will not achieve the intended objectives, or could lead to delays, and any of these changes could require the conduct of bridging studies and could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials. Additionally, the manner in which we currently manufacture our drug substance and product candidates and medical devices required to deliver such product candidates may not fulfill regulatory requirements for late-stage clinical trials and for commercial use, and there can be no assurance that we will be able to manufacture our drug substance and product candidates in a manner that would fulfill such regulatory requirements in a timely manner, or at all. We have limited experience in drug formulation or manufacturing. Currently, we rely on an extensive network of consultants and contract manufacturers, and in some cases sole source suppliers, for the production of our drug substance, product candidates and medical devices required to deliver such product candidates for current and planned clinical trials.

In order to conduct clinical trials of our product candidates, or supply commercial products, if approved, we will need to manufacture them and the drug substance contained in our product candidates in large quantities. Our CDMOs may be unable to successfully increase the manufacturing capacity for our drug substance and any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our CDMOs are unable to successfully scale up the manufacture of our drug substance or product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. The same risk would apply to our internal manufacturing facilities, should we decide to build internal manufacturing capacity in the future. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner, and the resources associated with ensuring the ongoing regulatory compliance of such manufacturing facilities would be significant.

In addition, the manufacturing process for any products that we may develop is subject to FDA, EMA, and comparable foreign regulatory authority approval processes and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA and foreign regulatory authority requirements, including complying with cGMPs on an ongoing basis. Although our agreements with our CDMOs require them to perform according to certain cGMP requirements such as those relating to quality control, quality assurance and qualified personnel, we cannot control the ability of our CDMOs to implement and maintain these standards. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA, EMA or other comparable foreign regulatory authorities or maintain a compliance status acceptable to the FDA, EMA, or other comparable foreign regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CDMOs will be able to manufacture the approved product to specifications acceptable to the FDA, EMA, or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods and have an adverse effect on our business, financial condition, results of operations and prospects.

If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates, and/or increase the product yield of its manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of our product candidates that we may develop, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third-party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the quality of the product, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operations.

We depend on third-party suppliers for key raw materials used in our manufacturing processes, as well as for the vaporization device used to administer GH001, and we expect to depend on third-party suppliers for the devices required for administration of GH002, some of which are our sole source of supply, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials or medical devices could harm our business.

We rely on our CDMOs to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical trials. We do not have, nor do we expect to enter into, any agreements for the commercial production of these raw materials, and we do not expect to have any control over the process or timing of our CDMOs' acquisition of raw materials needed to produce our product candidates. Furthermore, while our proprietary aerosol delivery device for GH001 has been approved for use in clinical trials by certain regulatory bodies, we currently purchase a vaporization device for use in our product bridging work from a single third-party manufacturer, Storz & Bickel, Tuttlingen.. We do not have a commercial supply agreement with such third-party manufacturer. Any significant delay in the supply of a product candidate, the raw material components thereof or any device necessary to administer our products for an ongoing clinical trial due to a manufacturer's need to replace a third-party supplier of raw materials or medical devices could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. Additionally, if our future manufacturers or we are unable to purchase these raw materials to commercially produce any of our product candidates that gains regulatory approvals, or if we are unable to purchase or manufacture medical devices with which we administer any of our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

A significant number of components in our proprietary aerosol delivery device for GH001 are manufactured in China. As such, if the relationship between China and Taiwan were to materially deteriorate, or if a trade war or other series of events were to occur that disrupted our supply chain for these raw materials, such changes could adversely affect our ability to conduct ongoing and future clinical trials of our product candidates, and/or adversely affect our ability to commercialize our products (subject to regulatory approval).

Furthermore, for those third-party suppliers who are our sole source of supply of certain materials, we may not have arrangements in place for a redundant or second-source supply of any such materials or medical devices in the event any of our current suppliers cease their operations for any reason. Establishing additional or replacement suppliers for the raw materials used in our product candidates or medical devices used to administer our product candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory inspection or approval, which could result in further delay.

We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

We are currently seeking and may continue to seek third-party collaborators for the research, development and commercialization of certain of the product candidates we may develop. Our likely collaborators include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs, or any product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce or defend intellectual property or proprietary rights relating to our product candidates or research programs, or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property-related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our product candidates or research programs that results from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates or research programs;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may control certain interactions with regulatory authorities, which may impact our ability to obtain and maintain regulatory approval of our product candidates;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may decide to not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may restrict us from researching, developing or commercializing certain products or technologies without their involvement;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may grant sublicenses to our technology or product candidates or undergo a change of control and the sublicensees or new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how or intellectual property of the collaborator relating to our products, product candidates or research programs;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our shareholders or disrupt our management and business;
- if our collaborators do not satisfy their obligations under our agreements with them, or if they terminate our collaborations with them, we may not be able to develop or commercialize product candidates as planned;
- collaborations may require us to share in development and commercialization costs pursuant to budgets that we do not fully control and our failure to share in such costs could have a detrimental impact on the collaboration or our ability to share in revenue generated under the collaboration;
- collaborations may be terminated in their entirety or with respect to certain product candidates or technologies and, if so terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or technologies; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished or terminated.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators could prevent us from receiving future payments under such agreements, which could negatively impact our revenues. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described herein also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions or alliances.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Employee Matters, Managing Our Business and Operations

We depend heavily on our executive officers, principal consultants and others, and the loss of their services would materially harm our business.

Our success depends, and will likely continue to depend, upon our ability to hire, retain the services of our current executive officers, principal consultants and others. The loss of their services might impede the achievement of our research, development and commercialization objectives. We do not maintain "key person" insurance for any of our executives or other employees.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. Replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully.

Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

We only have a limited number of employees to manage and operate our business. If we are unable to hire or to retain adequate personnel, then we may not be able to meet our operational goals.

As of December 31, 2025, we had employed seventy-three people and a large part of our development efforts remains outsourced to consultants, CMOs and CROs, aiming to optimize cash utilization and to manage and operate our business in a highly efficient manner. We cannot ensure that we will be able to hire and/or retain adequate staffing levels to develop GH001 and GH002 or other potential product candidates, or to run our operations and/or to accomplish all of the objectives that we otherwise would seek to accomplish.

Our employees, independent contractors, consultants, collaborators and CROs may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and CROs may engage in fraudulent conduct or other illegal activity. Misconduct by those parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates:

- regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities;
- manufacturing standards;
- federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities; and
- laws that require the accurate reporting of financial information or data.

Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our nonclinical studies or clinical trials or illegal misappropriation of product materials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this kind of activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, integrity oversight and reporting obligations, possible exclusion from participation in the United States in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations.

We expect to continue to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

Since our initial public offering, we have substantially expanded the size of our organization and we expect to continue to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of regulatory affairs and sales, marketing and distribution, as well as to support our public company operations. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Moreover, our expected growth could require us to relocate to a different geographic area of Ireland. Due to the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of existing and additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

Our business is subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability, in particular in foreign economies and markets;
- differing and changing regulatory requirements, price controls and reimbursement regimes;
- potentially reduced protection for our intellectual property rights;
- difficulties in compliance with different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations;
- changes in regulations and customs, tariffs and trade barriers;
- changes in currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by governments;
- negative consequences from changes in, including the interpretation of, tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States and the EEA;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- business interruptions resulting from geo-political actions, including war and terrorism, natural disasters including earthquakes, typhoons, floods and fires, or pandemics, epidemics, outbreaks of an infectious disease or similar events; and
- cyber-attacks, which are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect.

If a pandemic, epidemic, outbreak of an infectious disease or similar event occurs in Ireland or worldwide our business may be adversely affected. Such an event could delay enrollment in our clinical trials due to prioritization of hospital resources toward the outbreak or other factors, and some patients may be unwilling to enroll in our trials or be unable to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, which would delay our ability to conduct clinical trials or release clinical trial results and could delay our ability to obtain regulatory approval and commercialize our product candidates. Furthermore, such an outbreak could affect the operations of key governmental agencies, such as the FDA, EMA or other comparable foreign regulatory authorities, which could delay the development or approval process for any or all of our product candidates. The spread of a pandemic, epidemic, outbreak of an infectious disease or similar event may also result in the inability of our suppliers to deliver components or raw materials on a timely basis or at all. In addition, hospitals may reduce staffing and reduce or postpone certain treatments in response to an outbreak. Such events may result in a period of business disruption, and in reduced operations, or doctors and medical providers may be unwilling to participate in our clinical trials, any of which could materially affect our business, financial condition and results of operations. Finally, an ongoing outbreak of this nature may also cause the risks associated with our industry and business described herein and in our other public filings to become more significant. A significant pandemic, epidemic, outbreak of an infectious disease or similar event also could result in a widespread health crisis that could adversely affect the economies and financial markets worldwide, resulting in an economic downturn that could impact our business, financial condition and results of operations.

Additionally, a significant number of components in our proprietary aerosol delivery device for GH001 are manufactured in China. As such, if the relationship between China and Taiwan materially deteriorates, or if a trade war or other series of events occur that disrupt our supply chain for these raw materials, this could disrupt our supply chain, adversely affect our ability to conduct ongoing and future clinical trials of our product candidates, and/or adversely affect our ability to commercialize our products (subject to regulatory approval). For further information regarding risks to our supply chain from our international operations, see the risk factor titled "We depend on third-party suppliers for key raw materials used in our manufacturing processes, as well as for the vaporization device used to administer GH001, and we expect to depend on third-party suppliers for the devices required for administration of GH002, some of which are our sole source of supply, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials or medical devices could harm our business."

These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations.

Cyber-attacks or other failures in our telecommunications or IT systems, or those of our collaborators, CROs, third-party logistics or other service providers, distributors, suppliers or other contractors or consultants, could result in information theft, data corruption and significant disruption or unavailability of our business operations.

We, our collaborators, our CROs, third-party logistics and service providers, distributors, suppliers and other contractors and consultants utilize IT systems and networks to process, transmit and store electronic information in connection with our business activities. If our privacy, data protection, or information security measures (or those of any third parties that handle our sensitive information) are inadequate or are breached as a result of third-party action, employee or contractor error, malfeasance, malware, system error, software bugs or defects in our products, trickery, process failure or otherwise, third parties gaining access to employee accounts using stolen or inferred credentials, computer malware, viruses, spamming, phishing attacks or other means, and deliberate attacks and attempts to gain unauthorized access to computer systems and networks, and, as a result, there is improper disclosure of, or someone obtains unauthorized access to sensitive information, including personally identifiable information or protected health information, or if we suffer a ransomware or advanced persistent threat attack, or if any of the foregoing is reported or perceived to have occurred, our reputation and business could be damaged, we could incur significant costs associated with remediation and the implementation of additional security measures, we may incur significant liability and financial loss, and be subject to regulatory scrutiny, investigations, proceedings, lawsuits and penalties. While we are not aware of any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. These threats pose a risk to the security of our, our collaborators' and our CROs', third-party logistics and service providers', distributors', suppliers' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Any cyber-attack, data breach, inaccessibility or destruction or loss of data could result in a violation of applicable U.S. and international privacy, data protection and other laws, and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the United States and by international regulatory entities, resulting in exposure to material civil and/or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we are exposed and may not be adequate to indemnify us for all liability that may be imposed; and could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials for any of our product candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

Risks Related to the Ownership of Our Ordinary Shares

The market price of our ordinary shares has historically been, and in the future may continue to be, volatile and may fluctuate due to factors beyond our control, and you could lose all or part of your investment.

The price of the securities of publicly traded emerging pharmaceutical and drug discovery and development companies has been highly volatile and is likely to remain highly volatile in the future. In the past, we have experienced such volatility in the price of our ordinary shares. The market price of our ordinary shares could be subject to wide fluctuations in response to many risk factors, some of which are beyond our control, including the following:

- positive or negative results of testing and clinical trials by us, strategic partners or competitors;
- delays in entering into strategic relationships with respect to development or commercialization of our GH001 and GH002 product candidates or any other product candidates;
- entry into strategic relationships on terms that are not deemed to be favorable to us;
- regulatory restraints impacting development of current or future product candidates;
- technological innovations or commercial therapeutic introductions by competitors;
- changes in government regulations and healthcare payment systems;
- developments concerning proprietary rights, including patent and litigation matters;
- public concern relating to the commercial value or safety of any of our GH001 and GH002 product candidates or any other product candidates;
- negative publicity or public perception of the use of mebufotenin as a medical treatment;
- financing or other corporate transactions, or the failure to obtain financing or enter into other corporate transactions;
- publication of research reports or comments by securities or industry analysts;
- the trading volume of our ordinary shares on the Nasdaq Global Market (referred to herein as Nasdaq);
- sales of our ordinary shares by us, members of our senior management and directors or our shareholders or the anticipation that such sales may occur in the future;
- general market conditions in the pharmaceutical industry or in the economy as a whole;
- general economic, political, and market conditions and overall market volatility in the United States or the EU as a result of pandemics or similar events; and
- other events and factors, many of which are beyond our control.

These and other market and industry factors may cause the market price and demand for our securities to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their ordinary shares and may otherwise negatively affect the liquidity of our ordinary shares. In addition, pharmaceutical companies have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, including as a result of the COVID-19 pandemic.

Future sales, or the possibility of future sales, of our securities by existing shareholders could depress the market price of our ordinary shares.

Future sales of a substantial number of our ordinary shares, or the perception that such sales will occur, could harm the prevailing market price of our ordinary shares. These sales, or the perception that these sales could occur, also might make it more difficult for us to sell equity securities in the future and at a price that we deem appropriate.

Moreover, we have filed a registration statement on Form S-8 with the SEC covering ordinary shares available for future issuance under our equity incentive plans. While such registration statement remains effective, any ordinary shares issued under such plans will be eligible for sale in the public market, subject to compliance with Rule 144, in the case of our affiliates. Sales of a large number of the ordinary shares issued under these plans in the public market, or a perception that such sales may occur, could have an adverse effect on the market price of our ordinary shares. For more information on our equity incentive plans, see "Item 6. Directors, Senior Management and Employees—B. Compensation—Equity Incentive Plans".

Our executive officers, directors and certain significant shareholders will continue to own a substantial number of our ordinary shares and, as a result, may be able to exercise control over us, including the outcome of shareholder votes. Certain of our directors and officers hold interests in one of these shareholders and these shareholders may have different interests from us or your interests.

As of February 17, 2026, our officers, directors, 5% holders and their affiliates represented beneficial ownership, in the aggregate, of approximately 85.5% of our total outstanding ordinary shares, including 23.9% held by Florian Schönharting, the Chairman of our Board of Directors. As a result, these parties may be able to determine all matters requiring shareholder approval. For example, these shareholders may be able to exert control over our business, including significant corporate actions such as mergers, schemes of arrangement, sales of substantially all of our assets, and election, re-election and removal of directors. This may prevent or discourage unsolicited acquisition proposals or offers for our ordinary shares, or other such changes in control, that you may feel are in your best interest. The interests of this group of shareholders may not always coincide with your interests or the interests of other shareholders and they may act in a manner that advances their best interests and not necessarily those who purchase ordinary shares in the future, including seeking a premium value for their ordinary shares, and might affect the prevailing market price for our ordinary shares.

For more information regarding our principal shareholders and their affiliated entities, see "Item 7. Major Shareholders and Related Party Transactions —A. Major Shareholders".

The trading market for our ordinary shares is relatively illiquid, which may limit your ability to sell your shares.

Since our initial public offering, the trading market for our ordinary shares has been relatively illiquid. A public trading market having the desirable characteristics of depth, liquidity and orderliness depends upon the existence of willing buyers and sellers at any given time, such existence being dependent upon the individual decisions of buyers and sellers over which neither we nor any market maker has control. The failure of an active and liquid trading market to develop and continue would likely have a material adverse effect on the price of our ordinary shares. An inactive market may also impair our ability to raise capital to continue to fund operations through future equity issuances and may impair our ability to acquire other companies or technologies by using our shares as consideration in any such transactions.

We have never paid cash dividends, do not anticipate paying any cash dividends and our ability to pay dividends, or repurchase or redeem our ordinary shares, is limited by law.

We have never declared or paid cash dividends on our ordinary shares and do not anticipate paying any dividends on our ordinary shares in the foreseeable future. Any determination to pay dividends in the future will be at the sole discretion of our Board of Directors after considering our financial condition, results of operations, capital requirements, contractual restrictions, general business conditions and other factors our Board of Directors deems relevant, and subject to compliance with applicable laws, including the Irish Companies Act 2014 (as amended), (referred to herein as the Irish Companies Act), which requires Irish companies to have distributable reserves equal to or greater than the amount of the proposed dividend. Distributable reserves are the accumulated realized profits of the Company that have not previously been utilized in a distribution or capitalization less accumulated realized losses that have not previously been written off in a reduction or reorganization of capital. In addition, we cannot pay any dividend unless our net assets are not less than the aggregate of our called up share capital plus undistributable reserves and the dividend does not reduce our net assets below such aggregate. Undistributable reserves include the Company's undenominated capital (effectively its share premium and capital redemption reserve) and the amount by which the Company's accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed the Company's accumulated unrealized losses, so far as not previously written off in a reduction or reorganization of capital.

Unless the Company creates sufficient distributable reserves from its business activities, the creation of such distributable reserves would involve a reduction of the Company's share premium account or other undenominated capital account, which would require the approval of (i) 75% of our shareholders present and voting at a shareholder meeting, and (ii) the Irish High Court. In the event that we do not undertake a reduction of capital to create distributable reserves, no distributions by way of dividends, share repurchases or otherwise will be permitted under Irish law until such time as the Company has created sufficient distributable reserves from its business activities. The determination as to whether or not the Company has sufficient distributable reserves to fund a dividend must be made by reference to "relevant accounts" of the Company. The "relevant accounts" are either the last set of unconsolidated annual audited financial statements or unaudited financial statements prepared in accordance with the Irish Companies Act, which give a "true and fair view" of the Company's unconsolidated financial position in accordance with accepted accounting practice in Ireland.

We intend to retain earnings, if any, for use in our business and do not anticipate paying any cash dividends in the foreseeable future. As a result, capital appreciation, if any, on our ordinary shares will be an investor's sole source of gains for the foreseeable future. Any recommendation by our Board of Directors to pay dividends will depend on many factors, including our financial condition (including losses carried forward), results of operations, legal requirements and other factors. We are unlikely to pay dividends or other distributions in the foreseeable future.

Dividends paid may be subject to Irish dividend withholding tax.

We have never declared or paid cash dividends on our ordinary shares and do not anticipate paying any dividends on our ordinary shares in the foreseeable future. To the extent that we do make dividend payments (or other returns to shareholders that are treated as "distributions" for Irish tax purposes), in certain circumstances, as an Irish tax resident company, we will be required to deduct Irish dividend withholding tax (currently at the rate of 25%) from dividends paid to our shareholders. Shareholders that are resident in the United States, EU countries (other than Ireland) or other countries with which Ireland has signed a tax treaty (whether the treaty has been ratified or not) generally should not be subject to Irish dividend withholding tax so long as the shareholder has provided its broker, for onward transmission to our qualifying intermediary or other designated agent (in the case of shares held beneficially), or us or our transfer agent (in the case of shares held directly), with all the necessary documentation by the appropriate due date prior to payment of the dividend.

Our ordinary shares received by means of a gift or inheritance could be subject to Irish capital acquisitions tax.

Irish capital acquisitions tax, or CAT, could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares will be regarded as property situated in Ireland. The person who receives the gift or inheritance has primary liability for CAT. Gifts and inheritances passing between spouses are exempt from CAT, while children have a tax-free threshold of €400,000 in respect of taxable gifts or inheritances received from their parents. To the extent a person who receives a gift or inheritance involving our ordinary shares fails to qualify for an applicable exemption and/or surpasses the aforementioned threshold, such person could be liable for CAT.

If securities or industry analysts do not continue to publish research, or publish inaccurate or unfavorable research, about our business, the price of our ordinary shares and our trading volume could decline.

The trading market for our ordinary shares depends, in part, on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our ordinary shares or publish inaccurate or unfavorable research about our business, the price of our ordinary shares would likely decline. In addition, if our operating results fail to meet the forecast of analysts, the price of our ordinary shares would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our ordinary shares could decrease, which might cause the price of our ordinary shares and trading volume to decline.

Shareholders could be diluted in the future if we increase our issued share capital because of the disapplication of statutory preemption rights. In addition, shareholders in certain jurisdictions, including the United States, may not be able to exercise their preemption rights even if those rights have not been disapplied.

As a matter of Irish law, holders of our ordinary shares will have a preemption right with respect to any issuance of our ordinary shares for cash consideration or the granting of rights to subscribe for our ordinary shares for cash consideration, unless such preemption right is disapplied, in whole or in part, either in our Constitution (a copy of which is incorporated by reference as an Exhibit to this Annual Report) or by special resolution of our shareholders. The authorization of the directors to disapply such preemption rights must both be renewed by our shareholders at least every five years. Accordingly, at our annual general meeting of shareholders in 2025, our shareholders authorized our Board of Directors to opt out of these preemption rights as permitted under Irish law (for a period of five years, expiring on July 30, 2030). Thus, our Board of Directors will be permitted to issue up to all of our authorized but unissued share capital on a non-preemptive basis for cash consideration at any stage until 30 July 2030 (or such later data as approved by shareholders at a subsequent general meeting). In addition, even if the disapplication of preemption rights expires (and is not renewed by shareholders at a general meeting) or is terminated by our shareholders in a general meeting, due to laws and regulations in certain jurisdictions outside Ireland, shareholders in such jurisdictions may not be able to exercise their preemption rights unless we take action to register or otherwise qualify the rights offering under the laws of that jurisdiction. For example, in the United States, U.S. holders of our ordinary shares may not be able to exercise preemption rights unless a registration statement under the Securities Act is effective with respect to our ordinary shares issuable upon exercise of such rights or an exemption from the U.S. registration requirements is available. If shareholders in such jurisdictions are unable to exercise their preemption rights, their ownership interest would be diluted. Any future issuance of shares or debt instruments convertible into shares where preemption rights are not available or are excluded would result in the dilution of existing shareholders and reduce the earnings per share, which could have a material adverse effect on the price of shares.

We may be at an increased risk of securities class action litigation.

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical and biopharmaceutical companies have experienced significant share price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm the trading price of our ordinary shares.

A future transfer of ordinary shares, other than one effected by means of the transfer of book entry interests in DTC, may be subject to Irish stamp duty.

Transfers of ordinary shares effected by means of the transfer of book entry interests in the Depository Trust Company, or DTC, should not be subject to Irish stamp duty where ordinary shares are traded through DTC, either directly or through brokers that hold such shares on behalf of customers through DTC. However, if you hold your ordinary shares directly rather than beneficially through DTC, any transfer of ordinary shares could be subject to Irish stamp duty, subject to the availability of a relief or exemption (currently at the rate of 1% of the higher of the price paid or the market value of the shares acquired). Payment of Irish stamp duty is generally a legal obligation of the transferee. The potential for stamp duty to arise could adversely affect the price of our ordinary shares.

Ireland's Finance Act 2025 introduced a new exemption from Irish stamp duty (the "Market Capitalization Exemption") under section 86B of the Irish Stamp Duties Consolidation Act, 1999 (the "Stamp Duties Act") for transfers of shares in certain Irish incorporated companies where: (i) those shares are admitted to trading on a regulated market or multilateral trading facility (within the meaning of Directive 2014/65/EU of the European Parliament and of the Council of 15 May 2014 on markets in financial instruments and amending Directive 2002/92/EC and Directive 2011/61/EU) or a market located outside the European Union that is equivalent to a regulated market or multilateral trading facility; (ii) the closing market capitalization of the issuer is below the specified threshold of €1 billion on 1 December of the preceding year; and (iii) a valid notification has been made to the Irish Revenue Commissioners for the relevant year. Future transfers of our ordinary shares may be eligible for this exemption, subject to compliance with applicable notification requirements and other conditions under the Stamp Duties Act. There can be no assurance that we will qualify for this exemption in any particular year, or that the exemption will continue to be available, as eligibility depends on market capitalization thresholds, timely notification to the Irish Revenue Commissioners and other relevant conditions.

For more information, see "Item 10. Additional Information—E. Taxation—Material Irish Tax Consequences—Stamp Duty".

Our Constitution provides that the courts of Ireland will be the exclusive forum for the resolution of all shareholder complaints other than complaints asserting a cause of action arising under the Securities Act and the Exchange Act, and that the U.S. federal district courts will be the exclusive forum for the resolution of any shareholder complaint asserting a cause of action arising under the Securities Act and the Exchange Act.

Our Constitution provides that the courts of Ireland will be the exclusive forum for resolving all shareholder complaints other than shareholder complaints asserting a cause of action arising under the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act, and that the U.S. federal district courts will be the exclusive forum for resolving any shareholder complaint asserting a cause of action arising under the Securities Act and the Exchange Act. This choice of forum provision may limit a shareholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits. The enforceability of similar exclusive forum provisions (including exclusive federal forum provisions for actions, suits or proceedings asserting a cause of action arising under the Securities Act) in other companies' organizational documents has been challenged in legal proceedings, and there is uncertainty as to whether courts would enforce the exclusive forum provisions in our Constitution. Additionally, our shareholders cannot waive compliance with the federal securities laws and the rules and regulations thereunder. If a court were to find either choice of forum provision contained in our Constitution to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our results of operations and financial condition.

Claims of U.S. civil liabilities may not be enforceable against us.

We are incorporated and have our registered office in, and are currently existing under the laws of, Ireland. In addition, certain members of our Board of Directors and senior management are non-residents of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the securities laws of the United States. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws.

The United States and Ireland do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in Ireland. In addition, uncertainty exists as to whether Irish courts would entertain original actions brought in Ireland against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would be treated by Irish courts as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that certain requirements are met. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of U.S. securities laws, including whether the award of monetary damages under such laws would constitute a penalty is an issue subject to determination by the court making such decision. If an Irish court gives judgment for the sum payable under a U.S. judgment, the Irish judgment will be enforceable by methods generally available for this purpose. These methods generally permit the Irish court discretion to prescribe the manner of enforcement.

As a result, U.S. investors may not be able to enforce against us or our senior management, Board of Directors or certain experts named herein who are residents of Ireland or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

We believe that we were a PFIC for our 2025 taxable year, and we anticipate that we will likely be a PFIC in 2026 and potentially also in future years, which could subject U.S. investors in our ordinary shares to significant adverse U.S. federal income tax consequences.

Under the Internal Revenue Code of 1986, as amended, or the Code, we will be a PFIC for any taxable year in which, after the application of certain look-through rules with respect to our subsidiaries, either (1) 75% or more of our gross income consists of "passive income" or (2) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, "passive income." Passive income generally includes dividends, interest, certain non-active rents and royalties, and capital gains. Based on our current operations, income, assets and certain estimates and projections, including as to the relative values of our assets, including goodwill, which is based on the price of our ordinary shares, we believe that we were a PFIC for our 2025 taxable year due to the interest income we recognized (which is passive income for purposes of the PFIC rules) and the fact that we generated no other active income. Additionally, we expect a similar income composition in 2026 and, therefore, we anticipate that we will likely be a PFIC in 2026 and may also be a PFIC in future taxable years. However, because our PFIC status is a factual annual determination that can be made only after the end of the relevant taxable year, our PFIC status for 2026 or any future taxable year is uncertain. Prospective investors should invest in our ordinary shares only if they are willing to bear the U.S. federal income tax consequences associated with an investment in a PFIC.

If we are a PFIC for any taxable year during which a U.S. investor holds ordinary shares, we generally would continue to be treated as a PFIC with respect to that U.S. investor for all succeeding years during which the U.S. investor holds ordinary shares, even if we ceased to meet the threshold requirements for PFIC status. Such a U.S. investor would generally be subject to adverse U.S. federal income tax consequences, including (1) the treatment of all or a portion of any gain on disposition of the ordinary shares as ordinary income; (2) the application of a deferred interest charge on such gain and the receipt of certain dividends; and (3) certain reporting requirements. A "mark-to-market" election may be available that will alter the consequences of PFIC status if our ordinary shares are regularly traded on a qualified exchange. If we provide certain information to U.S. investors, a "qualified electing fund" election also may be available that will alter the consequences of PFIC status. For further discussion, see "Item 10. Additional Information—E. Taxation—Material U.S. Federal Income Tax Consequences for U.S. Holders".

We are an "emerging growth company" and are availing ourselves of reduced disclosure requirements applicable to emerging growth companies, which could make our ordinary shares less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and we intend to continue to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404(b) of the U.S. Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (1) the last day of the fiscal year (i) in which we have total annual gross revenue of $1.235 billion; (ii) the end of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering; or (iii) in which we are deemed to be a "large accelerated filer," which requires the market value of our ordinary shares that is held by non-affiliates to exceed $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three-year period. Investors may find our ordinary shares less attractive because we may rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and the price of our ordinary shares may be more volatile.

As a foreign private issuer, we are permitted to adopt certain home country requirements in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with corporate governance listing standards.

As a foreign private issuer, we are permitted to follow certain home country corporate governance requirements as opposed to those requirements that would otherwise be required by Nasdaq for domestic U.S. issuers. Following our home country governance practices allows us to follow Irish corporate law and the Irish Companies Act with regard to certain corporate governance matters as opposed to the requirements that would otherwise apply to U.S. companies listed on Nasdaq may provide less protection to our shareholders than what is accorded to investors under Nasdaq rules applicable to domestic U.S. issuers.

As a foreign private issuer, we are exempt from the rules and regulations under the Exchange Act related to the furnishing and content of proxy statements. Our officers, directors and principal shareholders are also exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. Pursuant to the National Defense Authorization Act for Fiscal Year 2026, our officers and directors will become subject to the reporting provisions contained in Section 16 of the Exchange Act beginning March 18, 2026. In addition, we are not required under the Exchange Act to file reports and financial statements with the SEC as frequently or as promptly as U.S. domestic companies whose securities are registered under the Exchange Act and we are exempt from filing quarterly reports with the SEC under the Exchange Act. Moreover, we are not required to comply with Regulation FD, which restricts the selective disclosure of material information, although we have voluntarily formed a disclosure committee consisting of certain of our officers to monitor and review disclosures made by the Company. These exemptions and leniencies will reduce the frequency and scope of information and protections to which you may otherwise have been eligible in relation to a U.S. domestic issuer.

We intend to continue to follow, or may in the future elect to follow, as the case may be, Irish corporate governance requirements in lieu of the corporate governance requirements of Nasdaq in respect of the following:

- the majority independent director requirement under Nasdaq listing rules;
- the requirement under Nasdaq listing rules that a compensation committee composed solely of independent directors governed by a compensation committee charter oversee executive compensation;
- the requirement under Nasdaq listing rules that director nominees be selected or recommended for selection by either a majority of the independent directors or a nominations committee composed solely of independent directors;
- the requirement under Nasdaq listing rules that a quorum must consist of at least $33^{1/3}$% of the outstanding shares of a listed company's common voting stock; and
- the requirement under Nasdaq listing rules that the independent directors have regularly scheduled meetings with only the independent directors present.

Furthermore, Nasdaq's corporate governance rules require listed U.S. companies to, among other things, seek shareholder approval for the implementation of certain equity compensation plans and issuances of ordinary shares, which we are not required to follow as a foreign private issuer. Therefore, our shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers. For further information, please see "Item 16G—Corporate Governance".

We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

While we currently qualify as a foreign private issuer, the determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter and, accordingly, the next determination will be made with respect to us on June 30, 2026.

In the future, we would lose our foreign private issuer status if we were to fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. For example, if more than 50% of our securities are held by U.S. residents and more than 50% of our executive officers or members of our Board of Directors are residents or citizens of the United States, we could lose our foreign private issuer status.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than costs we incur as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive in certain respects than the forms available to a foreign private issuer. In addition, we may lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers such as the ones described above and exemptions from procedural requirements related to the solicitation of proxies.

As a public company, we have incurred, and in the future will incur significant additional costs, and our management will be required to devote substantial time and attention to our public reporting obligations.

As a publicly traded company we have incurred, and in the future will incur significant additional legal, accounting and other expenses compared to levels when we were a private company. In addition, new and changing laws, regulations and standards relating to corporate governance and public disclosure, including the Dodd-Frank Wall Street Reform and Consumer Protection Act and the rules and regulations promulgated and to be promulgated thereunder, as well as under the Sarbanes-Oxley Act, the JOBS Act and the rules and regulations of the SEC and Nasdaq, have created uncertainty for public companies and increased our costs and time that our Board of Directors and management must devote to complying with these rules and regulations. We have invested, and intend to continue to invest, resources to comply with evolving laws, regulations and standards, and this investment has increased, and may continue to increase, legal and financial compliance costs and has diverted, and may continue to divert, management's time and attention from revenue-generating activities.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our securities.

You may have difficulties enforcing, in actions brought in courts in jurisdictions located outside the United States, judgments obtained in the U.S. courts under U.S. securities laws. In particular, if you sought to bring proceedings in Ireland based on U.S. securities laws, the Irish court might consider:

- that it did not have jurisdiction;
- that it was not the appropriate forum for such proceedings;
- that, applying Irish conflict of law rules, U.S. law (including U.S. securities laws) did not apply to the relationship between you and us or our directors and officers; or
- that the U.S. securities laws were of a penal nature and violated Irish public policy and should not be enforced by the Irish court.

It may not be possible to enforce court judgments obtained in the United States against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is some uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws. We have been advised that the United States currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on U.S. federal or state securities laws, would not automatically be enforceable in Ireland.

A judgment obtained against us will be enforced by the courts of Ireland only if the following general requirements are met:

- U.S. courts must have had jurisdiction in relation to the particular defendant according to Irish conflict of law rules (the submission to jurisdiction by the defendant would satisfy this rule); and

- the judgment must be final and conclusive and the decree must be final and unalterable in the court which pronounces it.

A judgment can be final and conclusive even if it is subject to appeal or even if an appeal is pending. But where the effect of lodging an appeal under the applicable law is to stay execution of the judgment, it is possible that in the meantime the judgment may not be actionable in Ireland. It remains to be determined whether final judgment given in default of appearance is final and conclusive. Irish courts may also refuse to enforce a judgment of the U.S. courts which meets the above requirements for one of the following reasons:

- the judgment is not for a definite sum of money;
- the judgment was obtained by fraud;
- the enforcement of the judgment in Ireland would be contrary to natural or constitutional justice;
- the judgment is contrary to Irish public policy or involves certain U.S. laws which will not be enforced in Ireland; or
- jurisdiction cannot be obtained by the Irish courts over the judgment debtors in the enforcement proceedings by personal service in Ireland or outside Ireland whether under Order 11 of the Irish Superior Courts Rules or otherwise.

As an Irish company, we are governed by the Irish Companies Act, which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our securities may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the United States.

You should also be aware that Irish law does not allow for any form of legal proceedings directly equivalent to the class action available in the United States. For further information with respect to your rights as a shareholder, see "Item 10. Additional Information—B. Memorandum and Articles of Association".

As an Irish public limited company, certain capital structure decisions require shareholder approval, which may limit our flexibility to manage our capital structure.

Under Irish law, our authorized share capital can be increased by an ordinary resolution of our shareholders and the directors may issue new ordinary shares up to a maximum amount equal to the authorized but unissued share capital, without shareholder approval, once authorized to do so by our Constitution or by an ordinary resolution of our shareholders. Additionally, subject to specified exceptions, Irish law grants statutory preemption rights to existing shareholders where shares are being issued for cash consideration but allows shareholders to disapply such statutory preemption rights either in our Constitution or by way of special resolution of our shareholders. Such disapplication can either be generally applicable or be in respect of a particular allotment of shares. The authorization of the directors to issue shares and the disapplication of statutory preemption rights must both be renewed by the shareholders at least every five years. Accordingly, at our annual general meeting of shareholders in 2025, our shareholders authorized our Board of Directors to issue ordinary shares up to the amount of our authorized share capital, and to opt out of the statutory pre-emption right for such issuances. Under Irish law, these authorizations will expire on July 30, 2030, five years after our shareholders renewed these authorizations. We cannot provide any assurance that these authorizations will always be approved, which could limit our ability to issue equity and thereby adversely affect the holders of our securities.

Provisions of our Constitution could delay or prevent a third party's effort to acquire us.

Our Constitution could delay, defer or prevent a third party from acquiring us, even where such a transaction would be beneficial to the holders of ordinary shares, or could otherwise adversely affect the price of ordinary shares. For example, certain provisions of our Constitution:

- impose advance notice requirements for shareholder proposals and director nominations to be considered at annual shareholder meetings; and
- require the approval of 75% of the voting power of our shares entitled to vote at a general meeting of shareholders to amend or repeal any provisions of our Constitution.

We believe these provisions, if implemented in compliance with applicable law, may provide some protection to holders of ordinary shares from coercive or otherwise unfair takeover tactics. These provisions are not intended to make us immune from takeovers. They will, however, apply even if some holders of ordinary shares consider an offer to be beneficial and could delay or prevent an acquisition that our Board of Directors determines is in the best interest of the holders of ordinary shares. Certain of these provisions may also prevent or discourage attempts to remove and replace incumbent directors.

In addition, mandatory provisions of Irish law could prevent or delay an acquisition of the Company by a third party. For example, Irish law does not permit shareholders of an Irish public limited company to take action by written consent with less than unanimous consent. In addition, an effort to acquire us may be subject to various provisions of Irish law relating to mandatory bids, voluntary bids, requirements to make a cash offer and minimum price requirements, as well as substantial acquisition rules and rules requiring the disclosure of interests in ordinary shares in certain circumstances.

Irish law differs from the laws in effect in the United States with respect to defending unwanted takeover proposals and may give our Board of Directors less ability to control negotiations with hostile offerors.

Following the authorization for trading of our ordinary shares on Nasdaq, we became subject to the Irish Takeover Panel Act, 1997, Irish Takeover Rules 2022, or the Irish Takeover Rules. Under the Irish Takeover Rules, our Board of Directors is not permitted to take any action that might frustrate an offer for our ordinary shares once our Board of Directors has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of shares, options, restricted share units or convertible securities by the Company, (ii) the redemption or repurchase of securities by the Company (save in certain circumstances) (iii) material acquisitions or disposals, (iv) entering into contracts other than in the ordinary course of business or (v) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our Board of Directors has reason to believe an offer is or may be imminent. These provisions may give our Board of Directors less ability to control negotiations with hostile offerors than would be the case for a corporation incorporated in a jurisdiction of the United States.

The operation of the Irish Takeover Rules may affect the ability of certain parties to acquire our ordinary shares.

Under the Irish Takeover Rules, if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30% or more of the voting rights of the company, the acquirer and, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for the outstanding ordinary shares at a price not less than the highest price paid for the ordinary shares by the acquirer or its concert parties during the previous 12 months. This requirement would also be triggered by an acquisition of ordinary shares by a person holding (together with its concert parties) ordinary shares that represent between 30% and 50% of the voting rights in the company if the effect of such acquisition were to increase that person's percentage of the voting rights by 0.05% within a 12-month period.

Under the Irish Takeover Rules, certain separate concert parties are presumed to be acting in concert. Our Board of Directors and their relevant family members, related trusts and "controlled companies" are presumed to be acting in concert with any corporate shareholder who holds 20% or more of our shares. The application of this presumption may result in restrictions upon the ability of any of the concert parties and/or members of our Board of Directors to acquire more of our securities, including under the terms of any executive incentive arrangements. We may consult with the Irish Takeover Panel with respect to the applicability of this presumption and the restrictions on the ability to acquire further securities without the requirement to make a mandatory offer to acquire all of our shares, although we are unable to provide any assurance as to whether the Irish Takeover Panel will overrule this presumption. Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares.

For a description of certain takeover provisions applicable to us, see "Item 10. Additional Information—B. Memorandum and Articles of Association—Anti-Takeover Provisions of Irish Law—Irish Takeover Rules and Substantial Acquisition Rules".

The operation of the Screening of Third Country Transactions Act 2023 of Ireland may affect the ability of certain parties to acquire our ordinary shares or to acquire certain of our assets.

The Screening of Third Country Transactions Act 2023 of Ireland, or the FDI Act established a foreign direct investment screening system in Ireland. The FDI Act requires parties to certain acquisition and/or investment transactions involving (i) Irish companies and business undertakings in a range of sectors (including critical health infrastructure); and (ii) acquiring/investing parties established in countries outside of the EEA and Switzerland, or third countries, to provide notice of such transactions to the Irish Minister for Enterprise, Trade and Employment for prior approval. The Minister will then determine if the relevant transaction poses a risk to Ireland's security or public order and may, where deemed appropriate, prevent the transaction from being consummated or otherwise impose conditions on the transaction. The Minister may also review transactions for which he/she has not received notice, if the Minister has reasonable grounds for believing that a given transaction poses a risk to Ireland's security or public order, whether such transaction has been completed or not. The FDI Act also results in increased information sharing and co-operation with other Member States of the EU in light of the EU Investment Screening Regulation (Regulation (EU) 2019/452). Accordingly, the application of the FDI Act may, if it applies to our activities, delay or restrict the ability of certain third parties outside of the EEA and Switzerland to acquire our ordinary shares or certain of our assets.

Risks Related to Our Controls Over Financial Reporting

Failure to maintain proper and effective internal control over financial reporting may hinder our ability to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ordinary shares.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We are required pursuant to Section 404 of the Sarbanes-Oxley Act to maintain internal control over financial reporting and to assess and report on the effectiveness of those controls. This assessment includes disclosure of any material weaknesses identified by our management in our internal control over financial reporting. Our management concluded that our internal controls over financial reporting were effective, as of the year ended December 31, 2025. For more information, see "Item 15. Controls and Procedures—B. Management's Annual Report on Internal Control Over Financial Reporting". However, any future failure to maintain adequate internal controls or produce accurate financial statements on a timely basis could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm the price of our ordinary shares.

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

GH Research PLC was incorporated as a public limited company under the laws of Ireland on March 29, 2021, to become a holding company for GH Research Ireland Limited. GH Research Ireland Limited was originally incorporated under the laws of Ireland on October 16, 2018, as GH Research Limited. GH Research Limited was re-registered as GH Research Ireland Limited on March 29, 2021. Our principal place of business is located at Joshua Dawson House, Dawson Street, Dublin 2, D02 RY95, Ireland, and our telephone number is + 353 1 437 8334. Our website address is www.ghres.com. We do not incorporate the information on or accessible through our website into this Annual Report, and you should not consider any information on, or that can be accessed through, our website as part of this Annual Report. We are required to file reports and other information with the U.S. Securities and Exchange Commission, or the SEC, including annual reports on Form 20-F and reports on Form 6-K. The SEC maintains an Internet site at *www.sec.gov* that contains reports, proxy and information statements and other information we have filed electronically with the SEC.

Our principal expenditures since January 1, 2023 have been our research and development expenses, as more fully described elsewhere in this Annual Report.

B. Business Overview

We are a clinical-stage biopharmaceutical company dedicated to transforming the lives of patients by developing a practice-changing treatment in depression. Our initial focus is on developing our novel and proprietary mebufotenin therapies for the treatment of patients with treatment-resistant depression, or TRD.

Our portfolio currently includes GH001, our proprietary inhalable mebufotenin product candidate and GH002, our proprietary intravenous mebufotenin product candidate. While GH001 is currently delivered via a vaporization device produced by a third party, we are developing a proprietary aerosol delivery device, which is currently in clinical investigation in Europe. We have completed two Phase 1 healthy volunteer clinical trials for GH001 (GH001-HV-101 and GH001-HV-103), in which administration of GH001 via inhalation was observed to be well tolerated at the investigated single dose levels and in an individualized dosing regimen, or IDR, with intra-subject dose escalation within a single day. We have also completed a Phase 1/2 clinical trial in patients with TRD (GH001-TRD-102) and a multi-center, randomized, double-blind, placebo-controlled Phase 2b trial with an Open-Label Extension of GH001 in patients with TRD (GH001-TRD-201). Based on observed clinical activity in these clinical trials, we believe that administration of GH001 has the potential to induce ultra-rapid remissions as measured by the Montgomery–Åsberg Depression Rating Scale, or MADRS in TRD patients.

Patients with major depressive disorder, or MDD, who have not adequately responded to therapy clearly have harder-to-treat depression, generally referred to as TRD. There is no consensus definition for TRD, but in the context of clinical trials, failure of at least one pharmacotherapy, one pharmacotherapy and one psychotherapy, or two pharmacotherapies has been used, the latter group having been referred to by regulatory authorities as patients with TRD. The Sequenced Treatment Alternatives to Relieve Depression, or STAR*D study, a collaborative study funded by the U.S. National Institute of Mental Health, demonstrated that approximately 37% of patients with MDD did not achieve a response despite two treatment steps. Based on this result we estimate that there are approximately nine million TRD patients in the United States and Europe who would be candidates for treatment. TRD has a greater economic and societal cost than non-TRD MDD. For instance, direct medical costs are approximately two- to threefold higher for TRD patients compared to non-TRD MDD patients.

Despite the significant unmet medical need in TRD and the substantial patient population, there are only two pharmacotherapies specifically approved for TRD in the United States: esketamine, as well as a combination of olanzapine and fluoxetine, an antipsychotic and antidepressant, respectively, both of which have shown mixed efficacy in clinical trials and are associated with potential side effects. Outside of pharmacotherapies, psychotherapies are also employed in the treatment of TRD, but involve a lengthy time commitment and are subject to large variability in availability, administration and effectiveness. Multiple forms of somatic intervention, such as transcranial magnetic stimulation, or rTMS, electroconvulsive therapy, or ECT, vagal nerve stimulation, or VNS, and deep brain stimulation, or DBS, are another common treatment approach for TRD, although these treatments are often deemed invasive and/or onerous, and there are limited data supporting long-term therapeutic benefit. Despite the range of treatments available for TRD, there is a large unmet medical need for new therapies to bring more patients into rapid and durable remissions and to reduce the associated social and economic burden.

Our goal is to develop and successfully commercialize novel and proprietary mebufotenin therapies for patients with TRD that are highly effective, rapidly acting, well tolerated and conveniently administered. We believe that various distinguishing features of our mebufotenin product candidates, including our lead product candidate GH001, will allow us to achieve those goals.

We believe that GH001, if approved, may provide significant benefits for the treatment of patients with TRD. We aim to achieve the following goals:

- maximization of ultra-rapid and durable remissions;
- single visit initial treatment, without additional mandated visits for psychotherapeutic intervention; and
- convenient and infrequent re-treatment.

Based on these features, we believe that GH001 could have the potential to provide an attractive alternative to currently available therapies and other therapies currently in development for the treatment of TRD.

Our Pipeline

We are developing our mebufotenin product candidates, GH001 and GH002, in our focus area of psychiatric and neurological disorders.

With our lead product candidate GH001, we have completed two Phase 1 clinical trials in healthy volunteers (GH001-HV-101 and GH001-HV-103), a Phase 1/2 trial in TRD (GH001-TRD-102) and two Phase 2a proof-of-concept trials, one in BDII and one in PPD. We have also completed our investigation of GH001 in a multi-center, randomized, double-blind, placebo-controlled Phase 2b trial (GH001-TRD-201) in TRD, which included a 6-month open-label extension. For our completed trials, we purchased a vaporization device from a third-party manufacturer with which we administered GH001. In 2021, we, with a contract development and manufacturing organization, or CDMO, initiated the development of a proprietary aerosol delivery device for GH001 for use in our pivotal clinical trial program, which we expect to initiate in 2026, and for commercial use. Based on our development progress, we submitted an investigational new drug application, or IND, for GH001, delivered with this proprietary device, to the U.S. Food and Drug Administration, or FDA, in August of 2023. As previously announced in September 2023, at the end of the 30-day statutory IND review period, the FDA advised us that it had placed our IND on clinical hold, and in October 2023, with a formal clinical hold letter, the FDA requested that we provide (i) an inhalation toxicology study in a non-rodent species and an additional inhalation toxicology study in rats, related to respiratory tract histology findings from a previously completed inhalation toxicology study in rats, (ii) additional device design verification information and (iii) updates to our investigator brochure. In November 2025, we submitted a complete response to the clinical hold and in December 2025, the hold was lifted by the FDA. In parallel, we are conducting the Phase 1 healthy volunteer clinical pharmacology trial (GH001-HV-106) using our proprietary device in the United Kingdom. GH002 is our second mebufotenin product candidate, formulated for administration via a proprietary intravenous injection approach. We have completed a randomized, double-blind, placebo-controlled, dose-ranging clinical pharmacology trial of GH002 in healthy volunteers (GH002-HV-105). We anticipate developing GH002 within our focus area of psychiatric and neurological disorders.

Our Strategy

Our mission is to develop novel proprietary mebufotenin therapies to induce ultra-rapid and durable remissions in patients with psychiatric and neurological disorders. In order to achieve this mission, key elements of our strategy include:

- Advancing GH001, our inhalable mebufotenin product candidate, for the treatment of TRD through clinical development, regulatory approval and commercialization, if approved;
- Evaluating additional opportunities for GH001 in psychiatric and neurological disorders;

- Advancing GH002, our intravenous mebufotenin product candidate through clinical development;
- Investigating additional delivery systems and additional routes of administration for mebufotenin;
- Expanding our intellectual property portfolio around mebufotenin; and
- Maximizing the value of our product portfolio by building internal commercialization infrastructure and entering selective partnerships.

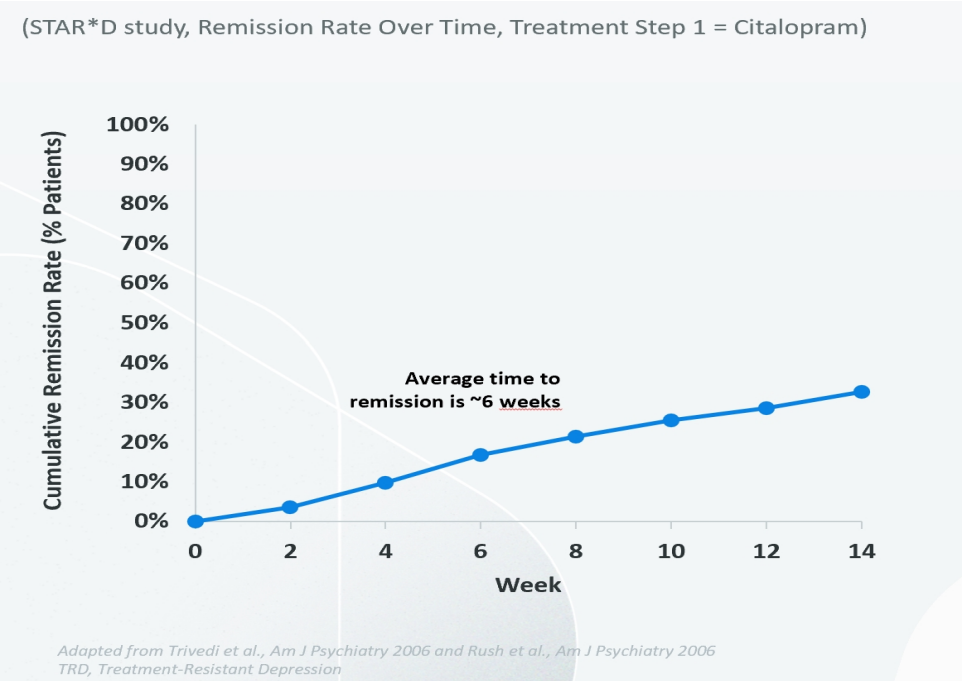
Our Market Opportunity

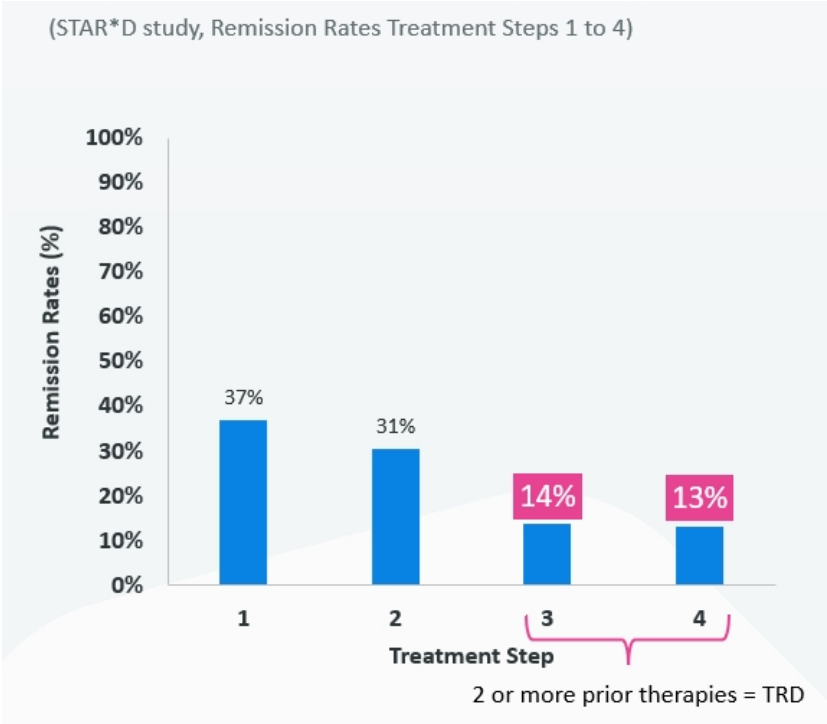
We are developing our mebufotenin product candidates for the treatment of a range of psychiatric and neurological disorders, with an initial focus on TRD, where there is a large unmet medical need. Our goal is to develop and successfully commercialize new therapies that are rapidly acting, highly effective, well tolerated and conveniently administered.

MDD and TRD Overview

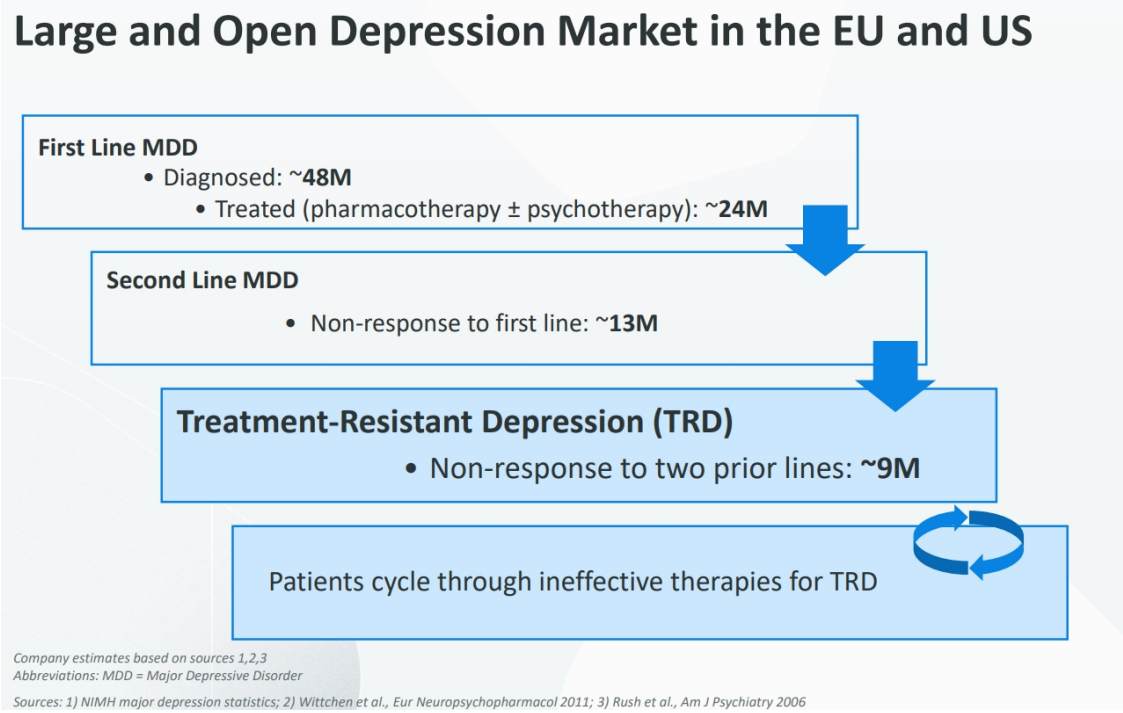
MDD is a serious mental health condition characterized by recurring episodes where feelings of sadness, loss of interest and other heightened negative emotions occur most of the day, nearly every day. MDD is associated with substantial morbidity, diminished quality of life and reduced life expectancy. The World Health Organization, or WHO, estimated that, as of 2015, more than 320 million people suffered from MDD worldwide and concluded that MDD is the single largest contributor to global disability, accounting for 7.5% of all years lived with disability.

Unfortunately, the efficacy of the existing anti-depressive treatments is limited by a slow onset of response, and a significant proportion of patients do not adequately respond even after multiple lines of therapy. The STAR*D study, a collaborative study funded by the U.S. National Institute of Mental Health, was designed to assess effectiveness of four subsequent treatment steps, which included both pharmacological and psychotherapeutic approaches, in a generalizable population of patients with depression. An American Journal of Psychiatry report on the STAR*D study by John Rush and co-authors summarized the acute and longer-term outcomes for all four successive treatment steps. The study reported both rates of remission, defined as a score of equal or less than 5 on the 16-item, clinician-rated Quick Inventory of Depressive Symptomatology, or QIDS-C16, and rates of response, defined as at least a 50% reduction in QIDS-C16 from treatment step entry. This STAR*D study found that remission rates were approximately 37%, 31%, 14% and 13% for the first, second, third and fourth treatment steps, respectively, and that the average time to remission in those who did remit across all treatment steps extended to about five to seven weeks. Approximately 33% of patients in the STAR*D study did not achieve a remission despite undergoing four treatment steps.


(STAR*D study, Remission Rate Over Time, Treatment Step 1 = Citalopram)
Cumulative Remission Rate (% Patients)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Average time to remission is ~6 weeks
0
2
4
6
8
10
12
14
Week
Adapted from Trivedi et al., Am J Psychiatry 2006 and Rush et al., Am J Psychiatry 2006
TRD, Treatment-Resistant Depression


(STAR*D study, Remission Rates Treatment Steps 1 to 4)
Remission Rates (%)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
37%
31%
14%
13%
1
2
3
4
Treatment Step
2 or more prior therapies = TRD

Patients with MDD who have not adequately responded to adequate therapy clearly have harder-to-treat depression, generally referred to as TRD. There is no consensus definition for TRD, but in the context of clinical trials, failure of at least one pharmacotherapy, one pharmacotherapy and one psychotherapy, or two pharmacotherapies have been used, the latter having been referred to by regulatory authorities as patients with TRD. The STAR*D study demonstrated that approximately 37% of patients with MDD did not achieve a response despite two treatment steps. Based on this result and based on an estimated number of approximately 48 million MDD patients in the United States and Europe according to the National Institute of Mental Health and an article published in European Neuropsychopharmacology, of which, according to the National Institute of Mental Health, about 50% receive treatment with pharmacotherapy or pharmacotherapy and psychotherapy, we estimate that there are approximately nine million TRD patients in the United States and Europe who would be candidates for treatment.



Despite this substantial patient population, only two pharmacotherapies have been approved specifically for the treatment of TRD in the United States: esketamine and a combination of olanzapine and fluoxetine, an antipsychotic and antidepressant, respectively.

Economic and Societal Burden

Global mental illness-associated costs, including direct costs associated with diagnosis, treatment and care and indirect costs associated with lost productivity and income, were estimated at $2.5 trillion for the year 2010, with the cost projected to surge to $6 trillion by 2030, whereby about two-thirds of the total cost comes from indirect costs, according to a report by the World Economic Forum and the Harvard School of Public Health. According to an article published in PharmacoEconomics in 2021, the annual economic burden of MDD alone in the United States is estimated to be US $326 billion (2018 estimate), up from $236 billion in 2010, with 35% being attributable to the direct costs of treatment, 4% to suicide-related costs, and 61% to indirect workplace costs. Per patient, TRD has a greater economic and societal cost than non-TRD MDD. TRD patients are often unable to perform daily tasks, are less productive at work and have higher rates of unemployment. They are also more likely to receive disability or welfare benefits and are reported to have a higher rate of co-occurring conditions, including diabetes, anemia and hypertension. Research conducted in 2018 and published in the Journal of Affective Disorders suggests that the proportion of patients suffering with TRD attempting suicide at least once during their lifetime could be as high as 30%.

According to a report published in the Journal of Affective Disorders, direct medical costs are approximately two- to threefold higher for TRD patients compared to non-TRD MDD patients. TRD patients have higher prescriptions costs, require more doctor visits and experience increased rates of hospitalization. They also have, on average, twice the number of inpatient visits compared with non-TRD MDD patients and their hospital stays are approximately 36% longer on average, according to an article published in the Journal of Clinical Psychiatry.

Existing Therapies for Depression

Because depression has a diverse set of biological, social, psychological, environmental, genetic and stress-related determinants, many of which co-occur, treatment options are wide-ranging and often combined. Current pharmacological and non-pharmacological treatments are efficacious only for a subset of MDD patients, and many patients do not respond or experience relapses. Clinicians lack high-quality evidence of whether certain therapies are suitable for certain patients and often rely on a lengthy trial-and-error approach, course-correcting as patients experience relapses or difficult side effects.

Pharmacotherapies

There are five main categories of antidepressants available. These are:

1. selective serotonin reuptake inhibitors, or SSRIs;

2. serotonin-norepinephrine reuptake inhibitors, or SNRIs;

3. atypical antidepressants;

4. monoamine oxidase inhibitors, or MAOIs; and

5. tricyclic antidepressants, or TCAs.

Antidepressants are frequently used in first- and second-line treatment of depression and can also be used after this point. As observed in the STAR*D study, only about 37% of patients achieve a remission with their initial antidepressant treatment. Failure rates of subsequent treatment regimens increase dramatically. For example, according to the STAR*D study, once patients have failed two lines of prior therapies, only about 14% of patients achieve a remission with their third antidepressant treatment, and less than 5% stay in remission for one year.

The current main categories of antidepressants have significant additional limitations, including slow onset of response, poor therapy adherence rates and various side effects. For the most commonly used antidepressants the average time to remission in those who remit extends to about five to seven weeks, according to the STAR*D study. Adherence levels are low, with less than 50% of individuals in primary and psychiatric care not adhering to their prescribed antidepressant medication after three months.

There is limited evidence to effectively guide clinical decisions following non-response or partial response to first-line antidepressant medications. Recommended treatment approaches include optimizing the current antidepressant dose or switching to another antidepressant. Partial response or lack of response thereafter is recommended to be addressed by combining antidepressants from different pharmacological classes or augmenting with an alternative medication, primarily with atypical antipsychotics but also mood stabilizers, anticonvulsants, thyroid hormones and stimulants.

Antipsychotics, such as olanzapine, quetiapine and aripiprazole, are typically used as adjunctive therapies when there is a lack of notable efficacy with an antidepressant. Despite there being an approved combination of olanzapine and fluoxetine for TRD that is administered once daily, research shows that combining antidepressants and antipsychotics can have serious side effects, such as weight gain, other metabolic complications, sedation, extrapyramidal side effects, which are drug-induced movement disorders, and QTc prolongation, which means the ventricles of the heart take longer than usual to recharge between beats.

Ketamine is an N-methyl-D-aspartate, or NMDA, receptor antagonist that has been used for several decades for sedation, anesthesia and chronic pain and is being used as an off-label treatment for TRD. The S-enantiomer of ketamine, esketamine, is administered via a nasal spray and was approved by the FDA in 2019 for the treatment of TRD (marketed as SPRAVATO® in the United States). While ketamine and esketamine treatments typically require frequent administration (for example, in the case of SPRAVATO®, a twice-weekly administration for 4 weeks, followed by weekly administration for 4 weeks, and then bi-weekly or frequent continuous administration, each in a controlled environment under medical supervision, with an estimated 40 administration visits per year), and while such administration is costly for payors and relatively burdensome for patients, recent improvements in patient access and the large unmet need have now supported broader clinical adoption.

Dextromethorphan, another NMDA receptor antagonist, which is also a sigma-1 receptor agonist, in combination with bupropion, an aminoketone and CYP450 2D6 inhibitor, administered as an oral tablet, was approved by the FDA in 2022 for the treatment of MDD and is marketed as AUVELITY® in the United States.

Psychotherapies

Psychotherapy is a form of talk therapy, which is often the preferred first-line treatment in patients with mild MDD. Psychotherapy is also used in combination with a pharmacotherapy, or as a substitute for pharmacotherapy, in patients with more severe MDD or in later-line treatments, including in patients with TRD. Two frequently used psychotherapies for depression are cognitive behavioral therapy, or CBT, and interpersonal therapy, or IPT. CBT focuses on changing negative thought and behavior patterns. IPT also assesses negative thoughts and behaviors, but only as they apply to interpersonal relationships and social functioning. Psychotherapeutic approaches can be effective for certain individuals but require a significant time commitment from patients and are subject to variability in their availability, delivery and effectiveness.

Somatic Therapies

Severe TRD patients who have undergone several courses of therapy are often treated with resource-intensive somatic therapies like ECT, rTMS, VNS, or DBS. These therapies are generally administered in inpatient settings. These treatments are typically reserved for patients who have not adequately responded to other treatments and are characterized as high-cost treatment options with limited reimbursement.

Summary

MDD is a serious mental health condition with substantial morbidity, diminished quality of life, reduced life expectancy and significant economic and societal burden. All of these issues are further accentuated in patients with TRD. Despite the availability of two pharmacotherapies approved specifically for the treatment of TRD in the United States, we believe currently available options do not adequately meet the needs of patients suffering from TRD and there is a significant need for a new therapeutic approach to bring more patients into rapid, durable remission.

We believe that the development of a safe, effective and convenient therapy for TRD is one of the biggest unmet needs and challenges in healthcare and that our mebufotenin product candidates, GH001 and GH002, have the potential to address this unmet need.

Bipolar Disorder (BD)

BD is a recurrent chronic affective disorder characterized by fluctuations in mood state and energy, affecting more than 10 million people in the United States and Europe, based on estimates of the National Institute of Mental Health and an article published in European Neuropsychopharmacology. The main characteristic separating BD from other affective disorders is the presence of recurring manic or hypomanic episodes that may alternate with depressive episodes. Although the symptoms come and go, BD usually requires lifelong treatment.

Bipolar I disorder, or BDI, is defined by the presence of overt manic episodes with a range of manifestations, including overconfidence, grandiosity, talkativeness, extreme disinhibition, irritability, decreased need for sleep, and highly elevated mood. Bipolar II disorder, or BDII, is characterized mainly by episodes of depression, but alternating with hypomania, a milder form of the overt mania in BDI. As defined by the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the lifetime presence of at least one manic episode is needed for the diagnosis of BDI and of at least one hypomanic episode and one major depressive episode is needed for the diagnosis of BDII.

Whereas hypomania is a milder form of mania, BDII is not generally perceived to be a milder form of BDI. Studies published in Archives of General Psychiatry on the natural course of BD found that BDII patients were symptomatic during 53.9% of follow-up weeks, with depressive symptoms present during 50.3% of follow-up weeks, while BDI patients were symptomatic during 47.3% of follow-up weeks with depressive symptoms present during 31.9% of follow-up weeks. It is evident that depressive symptoms dominate the symptomatic status in both types of BD, but most notably so in BDII. Evidence also suggests that a significant proportion of patients suffering from BD attempt suicide, with highest risk in phases with depressive symptoms and in patients with BDII.

Despite the disease burden of depressive symptoms in BDII, few studies have focused on the treatment of depression in BDII and only two drugs are specifically approved by the FDA for this indication, lumateperone and quetiapine. However, these treatments can be associated with significant side effects, such as somnolence, dizziness and dry mouth, they often exhibit delayed onset of response, which can take several weeks, and they have overall moderate efficacy. While other treatments are being used for depression in BDII, such as olanzapine combined with fluoxetine, lamotrigine or lithium, they suffer from similar limitations. Use of SSRIs is also frequent, however there is again only limited efficacy and an additional risk of induction of treatment-emergent mania or hypomania has been described.

In summary, depression is a major cause of suffering in BDII and there is a lack of safe, effective and rapid-acting agents for this condition. We believe that our mebufotenin product candidates, GH001 and GH002, have the potential to address this unmet need.

Postpartum Depression (PPD)

While more than 50% of women experience some form of low mood after childbirth, according to a 2021 article published in Translational Psychiatry, an estimated ~17% suffer from postpartum depression, or PPD, a debilitating disorder defined by the DSM-5 as a major depressive episode occurring during pregnancy or within 4 weeks following delivery.

In addition to experiencing symptoms commonly associated with major depression, PPD may lead to a wide range of negative consequences for the affected mother, her infant(s) and her family. For example, women with PPD may develop thoughts of self-harm or harming their child and they are at increased risk of suicide.

PPD may further lead to disruptions in the interactions between mother and child, exemplified by higher rates of disengaged behavior and lower rates of visual and vocal communication between mother and child, according to a 2010 article published in Infant Behavior and Development. Evidence also suggests an association between PPD and child development, as illustrated by the fact that children of patients suffering from PPD have a greater risk of impaired cognitive development, according to a 2003 article published in Archives of Women's Mental Health.

PPD is primarily treated via psychological therapies or pharmacotherapy, but for initiation of pharmacotherapies there is a higher threshold than in MDD, due to the changing risk-benefit ratio during pregnancy and breastfeeding, and breastfeeding mothers may be reluctant to commence pharmacological treatment due to a range of concerns.

Further, as in MDD, the efficacy of SSRIs is limited by a slow onset of response and a low remission rate, and significant side effects can occur. There are only two pharmacological therapies which are FDA-approved specifically for PPD, brexanolone, which requires a 60-hour infusion with in-patient admission and continuous monitoring by a healthcare provider, and zuranolone, which carries a warning regarding potential driving impairments due to central nervous system (CNS) depressant effects.

Hence, the burden of PPD is significant from multiple perspectives and there is a lack of safe, effective, rapid-acting and convenient agents for this condition. We believe that our mebufotenin product candidates, GH001 and GH002, have the potential to address this unmet need.

Our Mebufotenin Product Candidates

Inhalable Mebufotenin Product Candidate – GH001

Summary

Our lead mebufotenin product candidate, GH001, is formulated for administration via a proprietary inhalation approach. For GH001, we use synthetically developed, pharmaceutical grade mebufotenin free base, manufactured in accordance with current Good Manufacturing Practices, or cGMP, standards. We are currently investigating administration of GH001 as a single-dose regimen and in an IDR, where up to three escalating doses of GH001 are administered via inhalation on a single day. We have completed two Phase 1 healthy volunteer clinical trials for GH001 (GH001-HV-101 and GH001-HV-103), in which administration of GH001 via inhalation was observed to be well tolerated at the investigated single dose levels and in the IDR. We have also completed an open-label, single-arm Phase 1/2 trial in patients with TRD (GH001-TRD-102), two Phase 2a proof-of-concept trials, one in BDII and one in PPD, as well as a multi-center, randomized, double-blind, placebo-controlled Phase 2b clinical trial with an Open-Label Extension of GH001 in patients with TRD. We are currently investigating GH001 in a Phase 1 clinical pharmacology trial to evaluate our proprietary aerosol delivery device for administration of GH001 in healthy volunteers (GH001-HV-106).

Advantages of GH001

TRD is our lead indication for the development of GH001. We believe that GH001, if approved, may provide significant benefits for patients with TRD. We aim to achieve the following goals:

- maximization of ultra-rapid and durable remissions;
- single visit initial treatment, without additional mandated visits for psychotherapeutic intervention; and
- convenient and infrequent re-treatment.

Based on these features, we believe that GH001 has the potential to provide an attractive alternative to currently available therapies and other therapies in development for the treatment of TRD.

Completed Clinical Trials with GH001

Phase 1 Trials: GH001-HV-101, GH001-HV-103, GH001-TRD-102

We have completed three Phase 1 clinical trials with GH001, our inhalable mebufotenin product candidate.

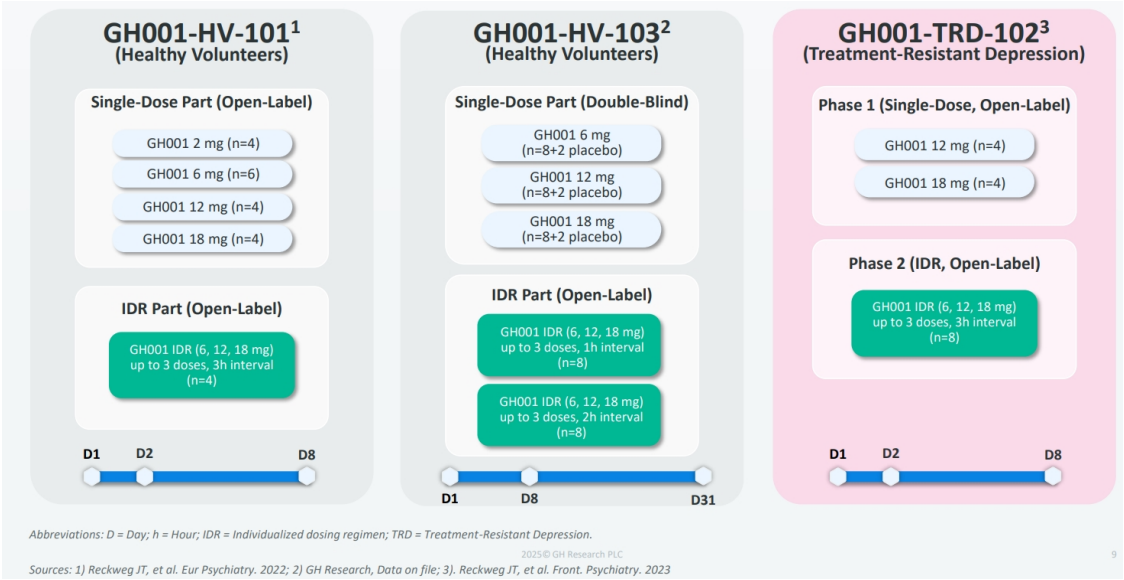
Trial Design

GH001-HV-101 (Healthy Volunteers) was designed in two parts: Part A was an open-label, single-arm, single-dose trial with four dose levels of GH001 being investigated and Part B was an open-label, single-arm, intra-subject dose escalation trial, where an IDR was administered on a single day with up to three increasing doses of GH001.

GH001-HV-103 (Healthy Volunteers) was designed in two parts: a single-dose part, in a double-blind, placebo-controlled, randomized, parallel-group design with single, inhaled doses of GH001 or placebo in 3 dose groups of 10 subjects, whereby 8 subjects per dose group received GH001 and 2 subjects per dose group received a placebo; and a multiple-dose part, in an open-label, non-randomized design, where our IDR was administered on a single day with up to three increasing doses of GH001.

GH001-TRD-102 (TRD Patients) was designed in two parts: Part A (n=8), which was an open-label, single-arm, single-dose Phase 1 trial with two dose levels of GH001 being investigated and Part B (n=8), which was an open-label, single-arm Phase 2 trial applying our IDR with intra-patient dose escalation with GH001.

In each trial, GH001 was administered at a single visit without additional mandated visits for psychological intervention.



Phase 1 Results: Safety (GH001-HV-101, GH001-HV-103, GH001-TRD-102)

In the three Phase 1 trials completed with GH001, 78 subjects were administered with GH001. Overall, inhalation of GH001 was well tolerated across the three trials with no severe or serious adverse events reported and with treatment emergent adverse events, or TEAEs, observed in 64.1% of subjects. The majority of TEAEs were mild in severity. No noteworthy changes in vital signs were observed; transient increases in heart rate and blood pressure shortly after GH001 administration were not considered clinically significant. Safety assessments, including laboratory analyses, psychiatric scales, electrocardiogram, and cognitive function tests showed no clinically meaningful changes. The most common TEAEs reported were: headache, anxiety, nausea and fatigue.

Safety Parameters, n (% of population)	Overall Population (n=78)
Any TEAE	50 (64%)
Headache	19 (24%)
Anxiety	12 (15%)
Nausea	8 (10%)
Fatigue	7 (9%)
Any Serious AE	0 (0%)
Any AE leading to trial/drug withdrawal	0 (0%)
Death	0 (0%)

TEAEs by Severity, no. of events	Overall Population (n=78)
Total number of TEAEs	105
Mild TEAEs	97
Moderate TEAEs	8
Severe TEAEs	0

Phase 1 Results: Efficacy (GH001-TRD-102)

As a secondary objective in Part A, we evaluated clinical activity, including MADRS remission, defined as a MADRS total score of less than or equal to 10, and MADRS clinical response, defined as a reduction of 50% or more from baseline in the MADRS total score. Two of four patients (50%) in the 12 mg group and one of four patients (25%) in the 18 mg group of Part A had a MADRS remission on Day 8, as well as a MADRS clinical response, and one further patient (25%) in the 18 mg group had a MADRS clinical response on Day 8. Of the three patients in remission on Day 8, all were in remission beginning on Day 2, with two in remission as early as two hours after dosing. The mean MADRS change from baseline at day seven was -21.0 (-65%) in the 12 mg group and -12.5 (-40%) in the 18 mg group.

The primary endpoint of Part B was defined as the proportion of patients in remission on day seven after dosing, defined as a MADRS total score of less than or equal to 10. This primary endpoint was met with seven of eight patients (87.5%) achieving a MADRS remission on Day 8 ($p<0.0001$). Of those seven patients, all were in remission beginning on Day 2, with four in remission as early as two hours after dosing. All seven patients with a remission on Day 8 also achieved a MADRS clinical response, defined as a reduction of 50% or more from baseline in the MADRS total score. The mean MADRS change from baseline at Day 8, a secondary endpoint, was -24.4 (-76%).

Phase 2a: Clinical Trial with GH001 in Patients with Bipolar II Disorder and a Current Major Depressive Episode (GH001-BD-202, NCT05839509)

We have completed a Phase 2a clinical trial in Europe with GH001 in patients with BDII and a current major depressive episode.

Trial Design

The trial was designed as an open-label, non-randomized, single arm trial, where our IDR was administered on a single day with up to 3 increasing doses of GH001 (6 mg, 12 mg, 18 mg). GH001 was administered without additional mandated visits for psychological intervention. The study enrolled 6 patients of the planned 15 patients.

The primary endpoint was to assess the effects on the severity of depression, as assessed by the mean change in MADRS from baseline to Day 8.

Results: Safety

All patients completed all planned visits. GH001 was well tolerated and no treatment-related serious adverse events were reported. The majority of TEAEs were mild or moderate and there were no reported TEAEs of hypomania or mania.

Results: Efficacy

The primary endpoint of the Phase 2a proof-of-concept trial for GH001 in BDII with a current major depressive episode was met with a significant reduction from baseline of –16.8 points (51.9%) in MADRS total score on Day 8 after administration of GH001 ($p=0.0099$). On Day 8, 33.3% of patients were in remission (MADRS ≤ 10).

GH001 led to an ultra-rapid antidepressant effect with a reduction in MADRS score at 2 hours after administration of –16.3 points ($p=0.0006$) and on Day 2 of -13.3 points ($p=0.0299$).

Phase 2a: Clinical Trial with GH001 in Female Patients with Postpartum Depression (GH001-PPD-203, NCT05804708)

We have completed a Phase 2a clinical trial in Europe with GH001 in female patients with PPD.

Trial Design

The trial was designed as an open-label, non-randomized, single arm trial, where our IDR was administered on a single day with up to 3 increasing doses of GH001 (6 mg, 12 mg, 18 mg). GH001 was administered without additional mandated visits psychological intervention. The study enrolled 10 patients of the planned 15 patients.

The primary endpoint was to assess the effects on the severity of depression, as assessed by the mean change in MADRS from baseline to Day 8.

Results: Safety

All patients completed all planned visits. GH001 was well tolerated and no treatment-related serious adverse events were reported. All TEAEs were mild or moderate.

Results: Efficacy

The primary endpoint of the Phase 2a proof-of-concept trial for GH001 in PPD was met with a significant reduction from baseline of –35.4 points (96.3%) in Montgomery–Åsberg Depression Rating Scale (MADRS) total score on Day 8 after administration of GH001 ($p<0.0001$). On Day 8, 100% of patients were in remission (MADRS ≤ 10).

GH001 led to an ultra-rapid antidepressant effect with a significant reduction in MADRS score at 2 hours after administration of –31.4 points ($p<0.0001$) and on Day 2 of –36.0 points ($p<0.0001$).

Phase 2b: Randomized, Double-Blind, Placebo-Controlled Clinical Trial with an Open-Label Extension of GH001 in Patients with TRD (GH001-TRD-201, NCT05800860)

We have completed an open-label extension part of a multi-center, randomized, double-blind, placebo-controlled Phase 2b clinical trial of GH001 in patients with TRD.

Trial Design

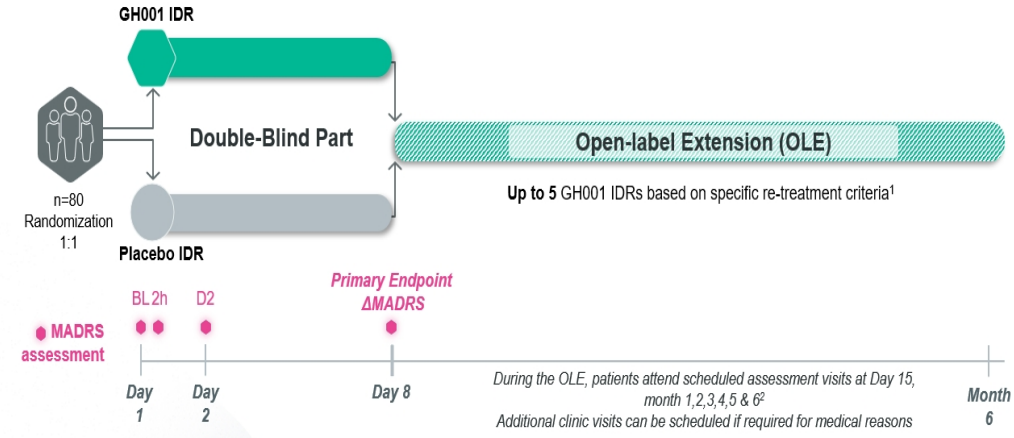
The trial consisted of two parts, as depicted below: Part 1, which was a 7-day randomized, double-blind, placebo-controlled phase, and Part 2, which was a 6-month open-label extension, or OLE, phase. The trial recruited 81 patients with TRD. In the double-blind, or DB, part, 40 patients received GH001 and 41 received placebo, with all patients directly transitioning into Part 2 on Day 8. Patients were administered an individualized dosing regimen, or IDR, of up to three escalating doses of GH001 or up to three doses of placebo on a single day. Psychotherapeutic intervention was not a component of either part of this trial. All patients in the trial had (i) moderate to severe depression, (ii) experienced a recurrent or single MDD episode (per DSM-5 criteria) without psychotic features, with a current episode of at least 2 years, (iii) failed between 2 and 5 antidepressants prior to enrollment and (iv) taken antidepressant treatments at least at the minimum applicable dose for at least 6 weeks.

In both parts, GH001 was administered as an IDR consisting of up to 3 increasing doses of GH001 (6 mg, 12 mg, and 18 mg) given at a planned 1-hour interval.

- In the DB Part 1, patients received either a single GH001 IDR or placebo IDR.
- In the OLE Part 2, patients received up to 5 GH001 IDRs as needed across 6 months, based on specific re-treatment criteria. Re-treatment criteria included the severity of depression and the effectiveness, tolerability and number of previous IDRs.

Patients between the ages of 18 to 64 years (inclusive) were eligible to be enrolled in the trial, with GH001 to be administered without additional mandated visits for psychological intervention.

The primary endpoint was to assess the effects on the severity of depression, as assessed by the mean change in MADRS from baseline to Day 8 at the end of the DB phase. The MADRS is a widely accepted scale for depression that ranges from zero to 60 that has been used as a primary endpoint in pivotal trials of other depression treatments. The FDA draft guidance for industry *"Major Depressive Disorder: Developing Drugs for Treatment"* highlights that for rapid-acting anti-depressants, efficacy generally should be demonstrated within 1 week for a rapid-acting antidepressant.



[1]Re-treatment criteria include the severity of depression and the effectiveness, tolerability, and number of previous IDRs. The patient meets one of the following criteria: i. has MADRS >18; or ii. has MADRS >10 and ≤18 and MADRS ≤10 has not been observed at D8 of the prior treatment or at any visit since then; or iii. has MADRS >10 and ≤18 and MADRS >18 has been observed since the most recent observation of MADRS ≤10
[2]Patients also attended assessment visits on Day 2 and Day 8 after each re-treatment
As in previously completed trials, the GH001-TRD-201 trial is conducted under the supervision of a healthcare provider, but without any planned psychotherapeutic interventions before, during, or after dosing.
Sources: 1) NCT05800860. (2024). A Trial of GH001 in Patients With Treatment-Resistant Depression. ClinicalTrials.gov. Accessed August 23, 2024.
Abbreviations: BL = Baseline; D = Day; h = Hour; IDR = Individualized dosing regimen; MADRS = Montgomery–Åsberg Depression Rating Scale; OLE = Open-label extension; TRD = Treatment-resistant depression.

DB Results: Patient Disposition and Characteristics

		GH001 (N=40)	Placebo (N=41)
Patient Disposition			
Completed double-blind part, n (%)		40 (100)	41 (100)
Discontinued double-blind part, n (%)		0 (0)	0 (0)
Age, years, mean (SD)		41.6 (11.4)	43.9 (10.9)
Female, n (%)		24 (60)	22 (53.7)
Race, white, n (%)		40 (100)	41 (100)
BMI, kg/m^2, mean (SD)		24.8 (4.3)	27.5 (6.3)
Previously used any psychedelic (lifetime)		4 (10)	5 (12.2)
Baseline Disease Characteristics			
HAM-D-17 Total Score, mean (SD)		24.9 (2.7)	24.6 (2.3)
MADRS Total Score, mean (SD)		29 (5.4)	28.2 (4.6)
Major Depressive Episode (MDE) History at Baseline			
Number of MDEs	Mean (SD)	2.1 (1.4)	2.0 (1.1)
	≥3, n (%)	14 (35.0)	13 (31.7)
Time since first depressive episode, years, mean (SD)		11.3 (9.7)	12.2 (8.4)
Duration of current MDE, weeks, mean (SD)		50.8 (28.3)	63.3 (106.9)
GH001 IDR Dose Received and Duration			
Total IDR dose received[1], n (%)	6 mg	9 (22.5)	0 (0)
	6, 12 mg	21 (52.5)	0 (0)
	6,12,18 mg	10 (25)	41 (100)
Duration of psychoactive effects, minutes, mean (SD)	6 mg (or PBO first dose)[2]	12.8 (9.1)	0.4 (2.3)
	12 mg (or PBO second dose)[2]	15.1 (9.8)	0.1 (0.8)
	18 mg (or PBO third dose)[2]	18.0 (15.2)	0.2 (1.1)

[1] For patients in the GH001/placebo groups, up to 3 doses of GH001 or placebo were administered;[2] Includes all patients who received respective dose of GH001/placebo, irrespective of total dose
Abbreviations: BMI = Body mass index; HAM-D-17 = Hamilton Rating Scale for Depression; MADRS = Montgomery-Åsberg Depression Rating Scale; MDE = Major Depressive Episode; IDR = Individualized dosing regimen; SD = Standard deviation; PBO = Placebo

DB Results: Safety

GH001 was well tolerated and no serious adverse events were reported in the DB part of the trial.

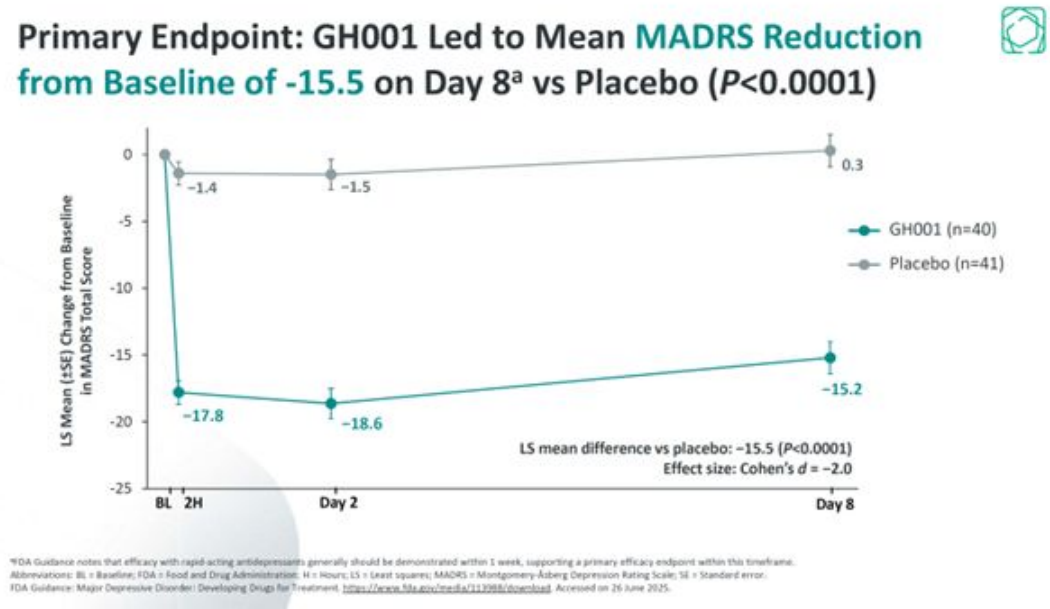
- All TEAEs were mild or moderate with no severe adverse events observed.
- The most common TEAEs in patients treated with GH001 were nausea, salivary hypersecretion, paresthesia, headache, and dysgeusia. There were no TEAEs of flashbacks reported.
- No clinically significant changes were observed in any of the safety laboratory analyses or vital parameters, including heart rate, blood pressure and ECG, and there were no adverse events, or AEs, related to vital signs.
- There were no TEAEs leading to study drug withdrawal or early withdrawal from the DB part of the trial.
- No dissociative state symptoms or sedation were observed at discharge after treatment with GH001 and 97.4% of patients were discharge ready within 1 hour of the last dose. Patients were not required to observe any post-discharge restrictions.
- No evidence of treatment-emergent suicidal ideation or behavior or treatment-emergent BPRS+ symptoms were observed after treatment with GH001.

Overview of Adverse Events: GH001 vs Placebo				
	GH001 N=40		Placebo N=41	
	Pts n (%)	Events n	Pts n (%)	Events n
Any TEAE[1]	29 (72.5)	81	3 (7.3)	7
Max severity of TEAEs[2]				
Mild	14 (35.0)	55	2 (4.9)	6
Moderate	15 (37.5)	26	1 (2.4)	1
Severe	0 (0)	0	0 (0)	0
Treatment-related TEAEs[3]	29 (72.5)	79	1 (2.4)	4
Device-related TEAEs	1 (2.5)	1	0 (0)	0
SAEs[4]	0 (0)	0	0 (0)	0
Treatment-related SAEs[3]	0 (0)	0	0 (0)	0
TEAEs leading to study drug withdrawal	0 (0)	0	0 (0)	0
TEAEs leading to early withdrawal from trial	0 (0)	0	0 (0)	0
AESIs	8 (20.0)	10	0 (0)	0
Death	0 (0)	0	0 (0)	0

[1]TEAE=AE that emerges after the start of study drug dosing having been absent pretreatment, or an AE that worsens in severity relative to a pretreatment onset
[2] Number of events for mild, moderate and severe TEAEs represents total number of events of each severity
[3]Treatment-related TEAE/SAE is any TEAE/SAE that is possibly or probably related to the study drug
[4]SAE=any untoward medical occurrence of effect at any dose that a) results in death, b) is life threatening, c) requires inpatient hospitalization or prolongation of hospitalization, d) results in persistent or significant disability or incapacity, e) is a congenital anomaly or birth defect, f) any other important medical event
Abbreviations: AESI = Adverse event of special interest; Pts = Patients; SAE = Serious adverse event; TEAE = Treatment-emergent adverse event; MedDRA = Medical dictionary for regulatory activities; PT = Preferred term

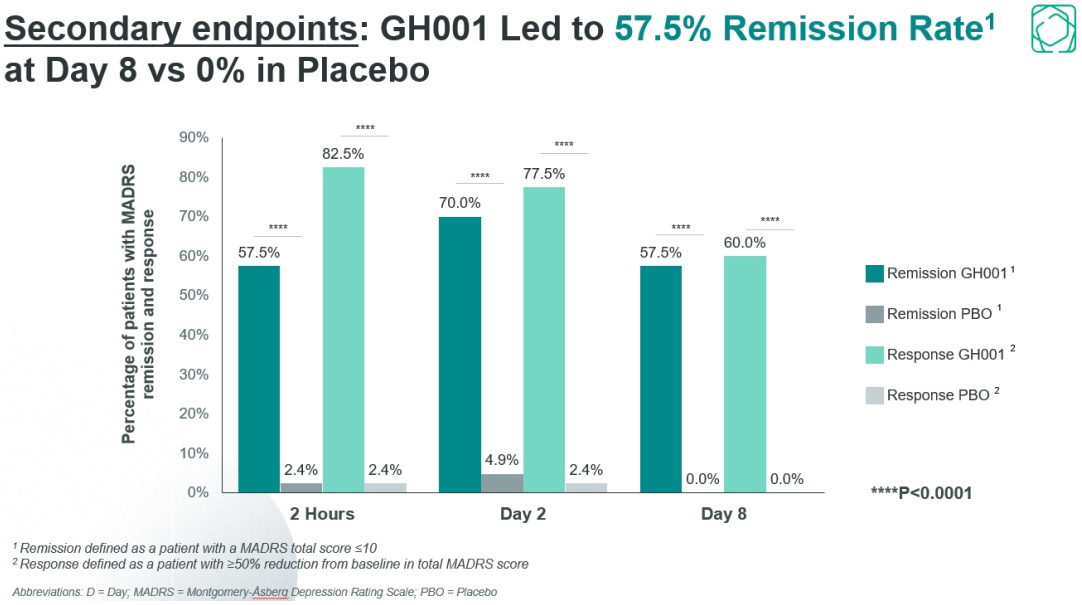
DB Results: Efficacy

As shown in the below figure, the primary endpoint of the trial was met with a significant reduction from baseline of -15.2 points in MADRS total score on Day 8 after administration of GH001, compared with +0.3 points in the placebo group (difference of -15.5 points, $p<0.0001$, Cohen's $d = 2.0$).



[a]FDA Guidance notes that efficacy with rapid-acting antidepressants generally should be demonstrated within 1 week, supporting a primary efficacy endpoint within this timeframe.
Abbreviations: BL = Baseline; FDA = Food and Drug Administration; H = Hours; LS = Least squares; MADRS = Montgomery-Åsberg Depression Rating Scale; SE = Standard error.
FDA Guidance: Major Depressive Disorder: Developing Drugs for Treatment. https://www.fda.gov/media/113988/download. Accessed on 26 June 2025.

All secondary endpoints in the trial were met, with results consistent with the primary endpoint**.** As shown in the below figure, the majority of the patients treated with GH001 achieved remission (MADRS≤10) and were responders (MADRS reduction ≥50%) at 2 hours, Day 2 and Day 8. Remission and response rates with GH001 were significantly greater than placebo at all timepoints (p<0.0001). Treatment with GH001 led to clinically and statistically significant improvements on the Clinical Global Impression Severity, or CGI-S, and Hamilton Anxiety Rating, or HAM-A, scales, and the Quality of Life Enjoyment and Satisfaction Questionnaire, or Q-LES-Q-SF Questionnaire, on Day 8, compared with placebo.



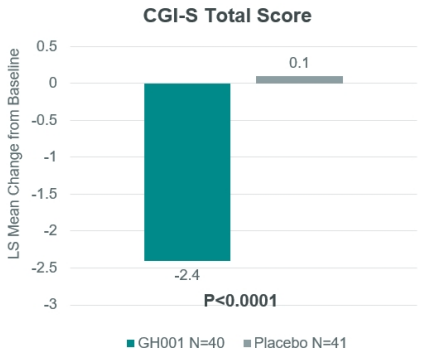
[1] Remission defined as a patient with a MADRS total score ≤10
[2] Response defined as a patient with ≥50% reduction from baseline in total MADRS score

Abbreviations: D = Day; MADRS = Montgomery-Åsberg Depression Rating Scale; PBO = Placebo

Secondary endpoints: GH001 led to CGI-S total score difference of -2.5 on Day 8 compared with placebo (p<0.0001)

CGI-S reflects the severity of the patient's illness as perceived by the clinician

CGI-S Results	GH001 (N=40)	Placebo (N=41)	P value
BL total score, mean (SD)	4.8 (0.7)	5.0 (0.6)	-
Day 8 total score, mean (SD)	2.4 (1.6)	5.0 (0.6)	-
LS mean (SE) change from BL to Day 8	**-2.4 (0.2)**	**0.1 (0.2)**	-
LS mean difference GH001 vs placebo	**-2.5 (0.3)**	-	**<0.0001**

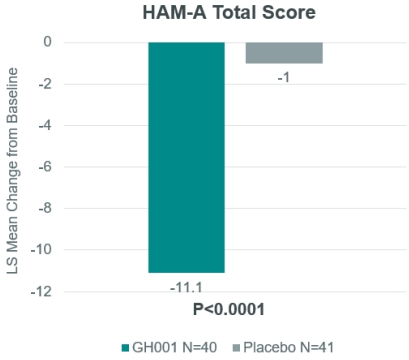


Abbreviations: BL = Baseline; CGI-S = Clinical Global Impression – Severity Scale Score; LS = Least squares; SD = Standard deviation; SE = Standard error.

Secondary endpoints: GH001 led to HAM-A total score difference of -10.0 on Day 8 compared with placebo (p<0.0001)

HAM-A assesses severity of anxiety symptoms

HAM-A results	GH001 (N=40)	Placebo (N=41)	P value
BL total score, mean (SD)	21.1 (6.5)	21.2 (6.1)	-
Day 8 total score, mean (SD)	10.0 (8.6)	20.1 (5.8)	-
LS mean (SE) change from BL to Day 8	**-11.1 (1.0)**	**-1.0 (1.0)**	
LS mean difference GH001 vs placebo	**-10.0 (1.4)**	-	**<0.0001**

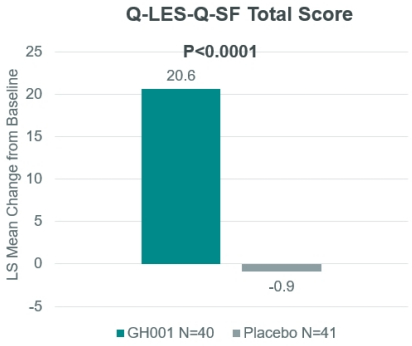


Abbreviations: BL= Baseline; HAM-A = Hamilton Anxiety Rating Scale; LS = Least squares; SD = Standard deviation; SE = Standard error.

Secondary endpoints: GH001 led to Q-LES-Q-SF total score difference of 21.5 on Day 8 compared with placebo (p<0.0001)

Q-LES-Q-SF measures QoL domains such as physical health, mood, work, household duties, schoolwork, leisure time activities, social and family relations, and overall well-being

Q-LES-Q-SF Results	GH001 (N=40)	Placebo (N=41)	P value
BL total score, mean (SD)	27.9 (9.0)	25.2 (8.2)	-
Day 8 total score, mean (SD)	47.2 (12.5)	25.5 (8.8)	-
LS mean (SE) change from BL to Day 8	**20.6 (1.8)**	**-0.9 (1.7)**	-
LS mean difference GH001 vs placebo	**21.5 (2.5)**	-	**<0.0001**



Abbreviations: BL = Baseline; LS = Least squares; Q-LES-Q-SF = Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form; QoL = Quality of Life; SD = Standard deviation; SE = Standard error.

Open-Label Results:

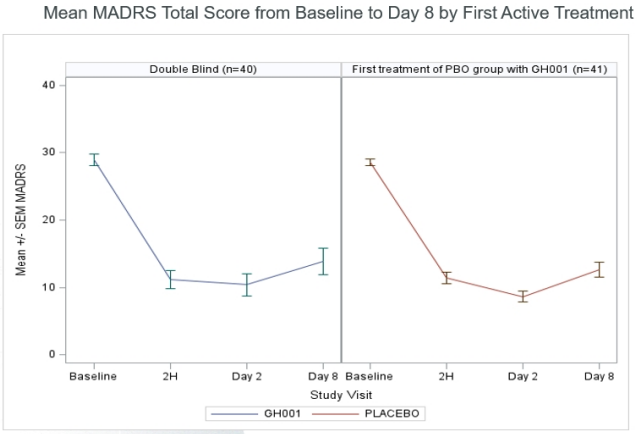
In the OLE part, 63 patients completed the full 6-month follow-up and 18 patients discontinued, with one patient's discontinuation due to an AE.

Of the 63 patients who completed the OLE:

- 73.0% of patients were in remission (MADRS≤10) at the 6-month visit and 79.4% were responders (MADRS reduction ≥50%), with an average of 4 treatments over the 6-month period;
- Mean MADRS total score at 6 months was 9.4;
- 63.5% (n=40) of patients received 1-4 treatments with GH001;
- 90.0% of patients who had remission at Day 8, also had remission at 6 months (patients who completed the 6-month OLE follow-up per protocol; patients who terminated early are excluded; n=63 patients in total).

Safety analysis confirmed that all patients from the DB part continued in the OLE and there were no treatment related serious adverse events during the full 6-month duration of the trial. No treatment-emergent events of suicidal intent or suicidal behavior occurred during the 6-month duration of the trial. The psychoactive experience had a median duration of 11 minutes across the DB and OLE parts of the trial.

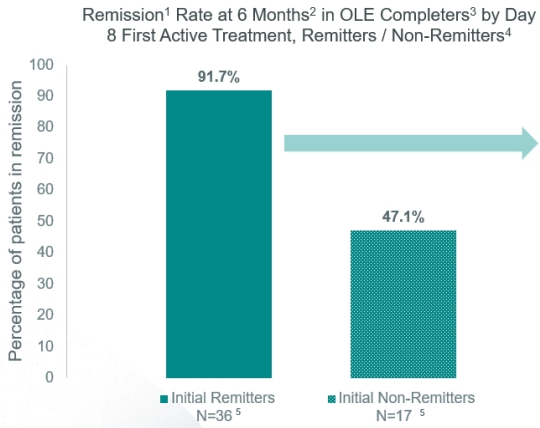
Reduction in MADRS total score with GH001 in DB reproduced in PBO Group with first GH001 treatment in OLE



- All patients enrolled in the DB part of the trial directly transitioned into the OLE at the end of the DB period.
- Once a patient completed the Day 8 visit of the DB part, if re-treatment criteria were met, a GH001 treatment could be administered.
- **All patients allocated placebo in the DB part received at least one treatment with GH001 in the OLE.**
- In the OLE, the reduction in MADRS total score in the DB placebo group following first active treatment*, was comparable to the results observed in the GH001 group in the DB part, showing **reproducibility of effects.**

*An active treatment refers to treatment with GH001
Abbreviations: BL = Baseline; DB = Double blind; MADRS = Montgomery-Åsberg Depression Rating Scale; SEM = Standard error of mean; PBO = Placebo; OLE = Open-Label Extension

Remission on Day 8 / Remission at 6 Months



Patients who had remission on Day 8 after their first active treatment had a 91.7% remission rate at 6 Months.

(91.7% of the OLE Completers[3] who had remission[1] at Day 8 after first active treatment[4], also had Remission at 6 Months[2].)

[1] Remission defined as a patient with a MADRS total score ≤10
[2] 6 Months' or 'Month 6' (end of trial) was at approximately 6 months post-study start (mean 168 days from Day 1 of double-blind period)
[3] Patients who completed the 6-month OLE follow-up per protocol (patients who terminated early are excluded)
[4] First active treatment refers to first treatment with GH001 = initial remitters / initial non-remitters
[5] N=53 patients in total; 1 OLE completer not evaluable due to missing data at data cut as of January 22, 2025

Across the DB and OLE, patients were deemed discharge ready by 1-hour from dose administration at 99% of treatment visits.

Ongoing Clinical Trials with GH001

Phase 1: Clinical Trial with GH001 aerosol delivery device in healthy subjects (GH001-HV-106, NCT06511947)

We are also currently recruiting an open-label Phase 1 trial to determine the pharmacokinetic, pharmacodynamics, and safety of GH001 administered via a proprietary aerosol delivery device in healthy subjects.

Trial Design

This is an open-label, Phase 1 clinical trial in healthy subjects that will include single- and multiple-dose parts. Following a screening period of up to 4 weeks prior to baseline, one single dose (Part 1), an IDR (Part 2), or two single doses (Part 3) of GH001 will be administered. In Part 1 and Part 2, GH001 will be administered via a proprietary aerosol delivery device on Day 1.

In Part 2, the IDR consists of up to three increasing doses of GH001 given at approximately 1-hour intervals.

The primary endpoint of this trial is to assess the pharmacokinetic profile of mebufotenin and bufotenine, a metabolite of mebufotenin, and safety and tolerability. Participants are monitored on the dosing day, with additional follow-up visits on Day 8 and Day 31.

Regulatory Interactions

Following a type C meeting with the FDA in May 2023, in August 2023 we submitted an IND for GH001, delivered with our proprietary aerosol delivery device, to the FDA. As previously announced in September 2023, at the end of the 30-day statutory IND review period, the FDA advised us that it had placed our IND on clinical hold, and in October 2023, with a formal clinical hold letter, the FDA requested that we provide (i) an inhalation toxicology study in a non-rodent species and an additional inhalation toxicology study in rats, related to respiratory tract histology findings from a previously completed inhalation toxicology study in rats, (ii) additional device design verification information and (iii) updates to our investigator brochure.

In November 2025, we met with the FDA and we submitted a complete response to the clinical hold and in December 2025, the hold was lifted by the FDA. The IND-opening trial will be a Phase 1 clinical trial in healthy volunteers to confirm the pharmacokinetics, pharmacodynamics and safety of GH001 delivered via our proprietary aerosol delivery device (GH001-HV-109).

Indication Expansion Opportunities for GH001

Given GH001's proposed mechanisms of resetting FC and serotonergic agonism, we believe that it represents a compelling therapeutic option for multiple psychiatric and neurological disorders other than TRD. Through collaborations with academic institutions and CROs we intend to explore the benefits of GH001 in additional psychiatric or neurological indications, the first of which are BDII and PPD.

Intravenous Mebufotenin Product Candidate - GH002

GH002 is our second mebufotenin product candidate, formulated for administration via a proprietary intravenous injectable approach. For GH002, we use a synthetically developed, pharmaceutical grade mebufotenin salt, manufactured in accordance with current cGMP standards. We believe GH002 has the potential to be an attractive therapeutic option, e.g., in patients with underlying airway or pulmonary disease or in situations where it is difficult to assure that the GH001 inhalation is performed adequately, such as in acute psychiatric emergency care situations where a patient may be unable to use an inhalation device.

Completed Clinical Trials with GH002

Phase 1: Clinical Pharmacology Trial with GH002 in Healthy Volunteers (GH002-HV-105, NCT05753956)

We have completed a Phase 1 clinical pharmacology trial of GH002 in healthy volunteers that was conducted in the Netherlands and top-line results are available.

Trial Design

The trial had two parts: a single-dose part, which was randomized, double-blind, placebo-controlled, with single, intravenous doses of GH002 or placebo in 7 dose groups (0.25 mg, 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, and 10 mg) of 8 subjects, whereby 6 subjects per dose group received GH002 and 2 subjects per dose group received a placebo; and a multiple-dose part, in an open-label, non-randomized design, where an IDR was administered to 8 subjects on a single day with up to 3 increasing doses of GH002 (2 mg as the first dose, 4 mg as the second dose and 6 mg as the third dose) with a scheduled 1-hour interval between doses. GH002 was administered without additional mandated visits for psychological intervention.

The primary endpoints of this trial were to assess the safety and tolerability and the pharmacokinetic profile of GH002. Participants were monitored on the dosing day, with an additional follow-up visit on Day 8.

Baseline Characteristics

56 subjects received single doses of 0.25 mg, 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, and 10 mg of GH002 (n=6 in each dose group), or placebo (n=2 in each dose group) in the single dose part of the trial, and 8 subjects received an IDR of up to three escalating doses of GH002 (2 mg, 4 mg, 6 mg) on a single day with a scheduled 1-hour interval between doses. The median age in the single-dose part was 23 years and in the multiple-dose part was 26.5 years. In the multiple-dose part, based on the IDR, four participants received 2 mg of GH002, two participants received 2 mg followed by 4 mg of GH002, and 2 participants received 2 mg, followed by 4 mg and then 6 mg of GH002.

Results

All participants completed all planned visits. No SAEs were reported. TEAEs were observed in 22 of 42 subjects (52%) who received GH002 and in 5 of 14 subjects (36%) who received placebo in the single-dose part, and in 4 of 8 subjects (50%) who received GH002 in the IDR part. The majority of TEAEs were mild. In the single-dose part, in subjects who received GH002, the most common TEAEs reported were: fatigue (in 6 participants), nausea (in 5 participants), dizziness (in 4 participants), vomiting and abdominal pain (each in 3 participants), emotional distress, head discomfort, headache, pain in extremity, muscles spasms, and grunting (each in 2 participants). In the IDR part, the most common TEAEs reported were: headache (in 2 participants), head discomfort, nausea, and vomiting (each in 1 participant).

No clinically relevant changes were observed in the safety laboratory analyses and ECG. With the exception of a temporary, non-clinically relevant increase in heart rate and blood pressure shortly after administration of GH002, no noteworthy changes in vital parameters occurred.

Potent PD effects as assessed by psychoactive effect (PsE) intensity were observed across single dose levels and the IDR, with an ultra-rapid onset of PsE and a short duration of the psychoactive experience (generally five to 30 minutes). The PK profile of GH002 was generally dose-linear and correlated with the ultra-rapid profile of the PsE. The analyses of the PK/PD relationship and other secondary endpoints are ongoing and awaited to inform the further clinical development strategy for GH002.

Conclusions

Intravenous administration of GH002 without additional psychological support before or after dosing, was observed to be well tolerated at the investigated single dose levels and in the IDR with intra-subject dose escalation with a scheduled 1-hour dose interval between doses, and potent and ultra-rapid PD effects as assessed by PsE intensity were observed.

Nonclinical Experience

Mebufotenin in vitro and in vivo data from published academic literature allowed initiation of our clinical trials GH001-HV-101, GH001-HV-103 and GH001-TRD-102. We have advanced a nonclinical study program with additional in vitro and in vivo toxicology studies as well as safety pharmacology studies, including studies evaluating genotoxicity and cardiotoxicity with our high-purity active pharmaceutical ingredient, or API, and an inhalation toxicology study in rats and an intravenous toxicology study in non-human primates. The results of these studies, together with the data from published academic literature, supported the initiation of our Phase 2a clinical trials of GH001 in BDII and a current major depressive episode (GH001-BD-202) and PPD (GH001-PPD-203), our Phase 2b clinical trial of GH001 in TRD (GH001-TRD-201), our Phase 1 clinical pharmacology trial of with our proprietary device (GH001-HV-106), and our Phase 1 clinical trial of GH002 in healthy volunteers (GH002-HV-105).

Further nonclinical studies are ongoing or expected to be performed in GH001 and/or other product candidates as our development progresses.

Delivery Systems and Routes of Administration for Mebufotenin

We are working to optimize current delivery systems and to investigate additional delivery systems and additional routes of administration for mebufotenin which we believe could expand the patient population that could benefit from our product candidates.

GH001, our inhalable mebufotenin product candidate, has been vaporized using an inhalation device purchased from a third party, which is a CE-marked medical device in the EU and licensed as a medical device in Canada and Australia. This device has been used in our Phase 2b trial in TRD patients (GH001-TRD-201) and in our completed Phase 2a trials in bipolar II disorder (GH001-BD-202) and postpartum depression (GH001-PDD-203). We have worked with a CDMO to develop a proprietary delivery device for GH001. Our proprietary device, as well as the third party device, is included in a Phase 1 clinical pharmacology trial in healthy volunteers (GH001-HV-106) designed to support bridging to the clinical data generated with the third-party device used in our completed clinical trials, following which we intend to use our proprietary device in our pivotal clinical trial program and for commercial supply. In advance of our pivotal program, we intend to execute a Phase 1 PK / PD study in the US under our open IND with our proprietary delivery device.

GH002, our intravenous mebufotenin product candidate, is currently administered using a standard, over-the-counter syringe. For future clinical studies we may license or acquire a specific delivery device from third parties or work with a CDMO to develop such device and establish manufacturing capabilities for such device.

We expect that GH001 along with the accompanying device, will be regulated by the FDA as a drug-device combination product. However, for GH002, this classification will depend on our final choice for its commercial presentation.

Manufacturing and Supply

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely on CDMOs to further develop and synthesize the API that is contained in our GH001 and GH002 product candidates and to further develop and manufacture our product candidates. The manufacturing processes are contracted so that the relevant API and product candidate manufacturing steps are compliant with cGxP. We expect to continue to rely upon third parties for the development and production of all clinical supply API and drug product that we may use. We also use contract manufacturers to fill, label, package, store and distribute our product candidates. We currently rely on two suppliers for each of our API and our GH001 product candidate, and because we maintain only a limited supply of API and GH001 product candidate we may not be able to avoid a material disruption in the event of any need to replace one or more of our suppliers. We are working with a CDMO to develop a proprietary delivery device for GH001 for use in our pivotal clinical trial program and for commercial use.

Commercialization

If either of our GH001 or GH002 product candidates are approved, we plan to use our own sales and marketing capabilities, targeting public and private healthcare providers and clinic networks and third-party payors in the United States and major European markets. However, depending on the situation, we may enter into commercialization collaborations, partnering or licensing agreements with third parties who have complementary commercial capabilities.

Competition

Our industry is characterized by many newly emerging and innovative technologies, intense competition and a strong emphasis on proprietary product rights. While we believe that our GH001 and GH002 product candidates represent a fundamental shift in the treatment paradigm relative to other TRD treatments on the market and under development, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, non-profit organizations, governmental agencies and medical research organizations. Any product candidates that we successfully develop and commercialize, including our GH001 and GH002 product candidates, will compete with the standard of care and new therapies, both pharmacological and somatic, which may become available in the future.

Based on the current understanding of regulatory agencies, TRD encompasses patients who have not been helped by two or more MDD pharmacotherapies. Currently, only two pharmacotherapies are approved specifically for TRD in the United States: SPRAVATO® (esketamine), marketed by Janssen, which is an NMDA receptor antagonist; and olanzapine and fluoxetine hydrochloride capsules, which are available generically. Because of this, antidepressants indicated for use in MDD are frequently prescribed, combined or augmented with a second agent to treat TRD patients. Several biopharmaceutical companies have therapies, including other tryptamine compounds, in preclinical and clinical development being evaluated or planned to be evaluated in mental illness, including in TRD patients, including AtaiBeckley, Axsome Therapeutics, COMPASS Pathways, Helus Pharma and Definium Therapeutics. Of the programs with other tryptamine compounds, the most advanced is COMPASS Pathways' investigational therapy COMP360 given in conjunction with psychological support, for which results of a Phase 2b trial in TRD have been reported and a Phase 3 program has been initiated.

Many of the pharmaceutical, biopharmaceutical and biotechnology companies with whom we may compete have established markets for their therapies and have substantially greater financial, technical, human and other resources than we do and may be better equipped to develop, manufacture and market superior and/or less expensive products or therapies. In addition, many of these potential competitors have significantly greater experience than we have in undertaking nonclinical studies and human clinical trials of new therapeutic substances and in obtaining regulatory approvals of human therapeutic products. Accordingly, our competitors may succeed in obtaining FDA or EMA approval for alternative or superior products. In addition, many competitors have greater name recognition and more extensive collaborative relationships. Smaller and earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Intellectual Property

Patent Strategy

Our commercial success is, in some part, linked to obtaining, maintaining and enforcing intellectual property rights protection in patents, trade secrets and other proprietary rights in the United States, EU and other jurisdictions. We plan to continue to strategically protect our innovations with parallel patent protection and regulatory and market exclusivity. We also may rely on trade secrets and know-how relating to our proprietary technologies, on continuing innovation and on future in-licensing opportunities to develop, strengthen and maintain the strength of our competitive position.

Issued Patents and Pending Patent Applications

Our patent portfolio includes at least 35 patent families directed to uses of mebufotenin including the use of mebufotenin for treatment of various disorders when administered by inhalation, or by nasal, buccal, sublingual, intravenous, intramuscular or subcutaneous routes, aerosol compositions of matter of mebufotenin, manufacturing methods for the preparation of and purification of mebufotenin, high purity mebufotenin, salt forms of mebufotenin and device-related aspects of mebufotenin administration. We are committed to exploring additional opportunities with mebufotenin through continuous research and development and will continue to seek patent protection for all our innovations.

Two of our patent families are directed to uses of mebufotenin for treatment of MDD and TRD, including when administered by inhalation, or by nasal, buccal, sublingual, intravenous, intramuscular or subcutaneous administration, respectively. These patent families include patents issued in at least, Europe, Japan and certain other jurisdictions outside of the United States. The issued patents in these families, and the pending patent applications, if issued, have expected expiry dates of no earlier than 2040, not including any patent term extensions and/or patent term adjustments.

Three of our patent families are directed to compositions of matter of mebufotenin, including high purity mebufotenin, the aerosol generated for the administration of GH001, and an HBr salt. These patent families include patents issued in the U.S. and Europe. The issued patents in these families, and the pending patent applications if issued, have expected expiry dates of no earlier than between 2040 and 2043, not including any patent term extensions and/or patent term adjustments.

At least 25 of our patent families are directed to various methods of use of mebufotenin, including use of mebufotenin to treat postpartum depression and bipolar disorder. The pending patent applications in these families, if issued, would have expected expiry dates of no earlier than 2043 or later, not including any patent term extensions and/or patent term adjustments.

Four of our patent families are directed to our proprietary device. The pending patent applications in these families, if issued, would have expected expiry dates of no earlier than 2044 or later, not including any patent term extensions and/or patent term adjustments.

We also own design patent applications directed to our proprietary device, one of which has been granted in the US, which is expected to expire in 2040, and one in Europe, which is expected to expire in 2049.

Two of our patent families are directed to manufacturing methods for the preparation of mebufotenin. These patent families include patents issued in at least Europe. The issued patents in these families, and the pending patent applications if issued, have expected expiry dates of no earlier than 2040.

In total, we have over 300 patent applications pending globally, including in the United States, Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, India, Japan, Korea, and Taiwan, as well as pending international applications under the Patent Cooperation Treaty, or PCT.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, record keeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or FDCA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, record keeping, approval, labeling, promotion and marketing, sale and distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products and medical devices. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as a clinical hold, FDA refusal to approve a pending new drug application, or NDA, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

Pharmaceutical product development for a new product in the United States, including a drug-device combination product, typically involves nonclinical laboratory and animal tests, the submission to the FDA of an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Nonclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the nonclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of nonclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, or product CMC, information about the device component of a drug-device combination product and a proposed clinical trial protocol. If clinical results are available from studies conducted outside the United States, that information must also be included in the IND. Long-term nonclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA places the trial on clinical hold. In such a case, the IND sponsor must correct the deficiencies cited in the hold letter or otherwise satisfy the FDA that the investigation may proceed before the clinical trial can begin. When the sponsor submits a complete response to the issues identified in the hold letter, the FDA must respond in writing to the sponsor within 30 days of the complete response by either removing or maintaining the clinical hold. The FDA can also place an IND on partial clinical hold, in which parts of the clinical work requested may proceed, but other parts are delayed or suspended until the FDA's outstanding concerns are resolved.

Clinical trials involve the administration of the IND to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted (i) in compliance with federal regulations; (ii) in compliance with Good Clinical Practices, or GCPs, which are standards meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may be combined or overlap. Phase 1 involves the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial may be sufficient in rare instances, including (i) where the study is a large multi-center trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible or (ii) when in conjunction with other confirmatory evidence.

The manufacturer of an investigational drug in a Phase 2 or 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all nonclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. In the case of a drug-device combination product, the NDA must also include design, testing, manufacturing and quality information to support the device constituent, including information to support its use and compatibility with the drug constituent. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, and the applicant under an approved NDA is also subject to an annual program fee. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be filed based on the FDA's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is filed, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most applications for standard review drug products that are new molecular entities, or NMEs, are reviewed within 10 months of the date that the FDA files the NDA; most applications for priority review drugs that are NMEs are reviewed within six months of the date that the FDA files the NDA. Priority review can be applied to drugs that the FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP. Additionally, the FDA will generally inspect the facility or the facilities at which the drug and in the case of a drug-device combination product, the device constituent, is manufactured. The FDA will not approve the product unless compliance with cGMPs is satisfactory and the NDA contains data that demonstrate that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Combination Products

A combination product is a product comprising (i) two or more regulated components, i.e., drug-device, biologic-device, drug/biologic or drug-device/biologic, that are physically, chemically or otherwise combined or mixed and produced as a single entity; (ii) two or more separate products packaged together in a single package or as a unit and comprising drug and device products, device and biological products or biological and drug products; (iii) a drug, device or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device or biological product where both are required to achieve the intended use, indication or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, for example, to reflect a change in intended use, dosage form, strength, route of administration or significant change in dose; or (iv) any investigational drug, device or biological product packaged separately that, according to its proposed labeling, is for use only with another individually specified investigational drug, device or biological product where both are required to achieve the intended use, indication or effect.

The FDA is divided into various branches, or Centers, by product type. Different Centers typically review drug, biologic or device applications. In order to review an application for a combination product, the FDA must decide which Center should be responsible for the review. FDA regulations require that the FDA determine the combination product's primary mode of action, which is the single mode of a combination product that provides the most important therapeutic action of the combination product. The Center that regulates that portion of the product becomes the lead evaluator. When evaluating an application, a lead Center may consult other Centers but still retain complete reviewing authority, or it may collaborate with another Center, by which the Center assigns review of a specific section of the application to another Center, delegating its review authority for that section. Typically, an applicant submits a single marketing application to the Center selected to be the lead evaluator, although separate applications for each constituent part may be submitted to the applicable Centers. One reason to submit multiple evaluations is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each may be evaluated by a different lead Center.

In a drug-device combination product, where the device component is a pre-filled drug delivery device, the primary mode of action is typically a drug mode of action with the Center for Drug Evaluation and Research, or CDER, as the lead Center. CDER would review the NDA in consultation with the Center for Devices and Radiological Health on device-specific issues. For co-packaged or single entity combination products, such as pre-filled drug delivery devices, there are two ways to comply with cGMP requirements. Manufacturers can either (i) demonstrate compliance with all cGMP regulations applicable to each of the constituent parts in the combination product or (ii) in the case of drug-device combination products, demonstrate compliance with either the drug cGMP regulations or the device quality management system requirements, or device QMSR, and also demonstrate compliance with additional provisions from the other of these two sets of cGMP requirements, as specified in the combination products regulations.

Failure to comply with applicable regulatory requirements can result in enforcement action by the FDA, which may include any of the following sanctions: warning or untitled letters, fines, injunctions, civil or criminal penalties, recall or seizure of current or future products, operating restrictions, partial suspension or total shutdown of production, refusal or denial of submissions for new products or withdrawal of clearance, authorization or approval.

Expedited Development and Review Programs for Drugs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track Designation, Breakthrough Therapy Designation, Priority Review and Accelerated Approval, and the purpose of these programs is to either expedite the development or review of important new drugs.

A drug is eligible for Fast Track Designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track Designation provides increased opportunities for sponsor interactions with the FDA during nonclinical and clinical development, in addition to the potential for rolling review of a marketing application. Rolling review means that the Agency may review portions of the marketing application before the sponsor submits the complete application, though the review clock does not begin until all portions of the application have been submitted.

In addition, a drug may be eligible for Breakthrough Therapy Designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy Designation provides all the features of Fast Track Designation in addition to intensive guidance on an efficient drug development program and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy Designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including Priority Review designation and Accelerated Approval. A product is eligible for Priority Review designation, once an NDA is submitted, if the drug that is the subject of the marketing application has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. If the FDA grants priority review, the FDA's goal date to take action on the marketing application is six months compared to 10 months for a standard review.

A product is eligible for Accelerated Approval if it can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Accelerated Approval is contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit. These confirmatory trials must be completed with due diligence, and, in most cases, the FDA may require that the trial be designed, initiated and/or fully enrolled prior to approval. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. In addition, the FDA generally requires, as a condition for Accelerated Approval, that all advertising and promotional materials intended for dissemination or publication be submitted to the FDA for review.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, Fast Track Designation, Breakthrough Therapy Designation, Priority Review and Accelerated Approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval, though they may expedite the development or review process.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to products intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States or more than 200,000 individuals in the United States but for which there is no reasonable expectation that the cost of developing and making the product for this type of disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The first NDA applicant to receive FDA approval for a particular active moiety to treat a rare disease for which it has such designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care, or in instances of drug supply issues. Orphan drug exclusivity does not prevent FDA from approving a different drug for the same disease or condition or the same drug for a different disease or condition. Other benefits of orphan drug designation include tax credits for certain research and an exemption from the NDA application fee.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information on ClinicalTrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric Information

Under the Pediatric Research Equity Act, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant full or partial waivers or deferrals for submission of data.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity—patent or non-patent—for a drug if certain conditions are met. Conditions for exclusivity include the FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric studies and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing or if previously unrecognized problems are subsequently discovered.

The FDA strictly regulates marketing, labeling, advertising and promotion of drugs that are placed on the market. Advertising and promotion of drugs must be in compliance with the FDCA and its implementing regulations and only for the approved indications and in a manner consistent with the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities.

The Hatch-Waxman Act

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an Abbreviated New Drug Application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, nonclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a statement certifying that its proposed ANDA label does not contain (or carve out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

To the extent that a Section 505(b)(2) applicant is relying on the FDA's prior findings of safety or effectiveness for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Thus, approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Exclusivity

Upon NDA approval of a new chemical entity, which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which the FDA cannot receive any ANDA seeking approval of a generic version of that drug. An ANDA may be submitted one year before new chemical entity exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period. Certain changes to a drug, such as the addition of a new indication to the package insert, can be the subject of a three-year period of exclusivity if the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to approval of the application. The FDA cannot approve an ANDA for a generic drug that includes the change during the exclusivity period.

The FDCA alternatively provides three years of marketing exclusivity for an NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval), up to a maximum of five years. The extension period can be shortened if, among other things, the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years, and only one patent can be extended. For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. To obtain interim patent extension, the director of the United States Patent and Trademark Office, or USPTO, must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Controlled Substances

The federal Controlled Substances Act, or CSA, and its implementing regulations establish a "closed system" of manufacture and distribution of controlled substances. The CSA and regulations promulgated by the U.S. Drug Enforcement Administration, or DEA, impose registration, security, record keeping and reporting, storage and other requirements on individuals and other entities that handle controlled substances. The DEA is the federal agency responsible for regulating controlled substances and requires those individuals or entities that manufacture, import, export, distribute, research or dispense controlled substances to comply with the regulatory requirements in order to promote legitimate use of controlled substances and prevent the abuse and diversion of controlled substances to illicit channels of commerce.

The DEA categorizes controlled substances into one of five schedules—Schedule I, II, III, IV or V—depending on the relative potential for dependence and abuse. Schedule I substances by definition have the highest potential for abuse, have no currently accepted medical use in treatment in the United States and lack accepted safety for use under medical supervision. Pharmaceutical products demonstrating some abuse potential but that do have a currently accepted medical use and are approved for marketing are classified in Schedule II, III, IV or V depending on abuse potential. Among controlled substances that can be marketed, Schedule II substances are considered to have the highest potential for abuse and physical or psychological dependence, and Schedule V substances the lowest relative potential for abuse and dependence.

Mebufotenin is currently classified as a Schedule I drug and, if the substance or a formulation containing the substance is approved for marketing in the United States, will need to be rescheduled from Schedule I to either Schedule II, III, IV or V by the DEA before it can be commercially marketed, distributed and sold. Rescheduling is dependent on FDA approval and the FDA must make a recommendation to the DEA on the appropriate schedule. The DEA must conduct notice and comment rulemaking to reschedule any controlled substance. Such action is subject to public comment and potential requests for an administrative hearing objecting to, or supporting, any such action. In addition, because each state has its own statutory and regulatory requirements related to controlled substances, each state or jurisdiction must also take appropriate administrative or legislative action to reschedule a controlled substance within that state based on federal rescheduling.

A DEA registration is required for all manufacturers, importers, exporters and distributors who must register annually with the DEA to handle controlled substances. A DEA registration is also required for pharmacies and physicians who prescribe, administer and/or dispense controlled substances; they must register every three years. The DEA registration is specific to each facility (i.e., physical location) and the activity(ies) and controlled substance schedule(s) handled at each location.

The DEA conducts cyclic inspections all manufacturing, importing, exporting and distribution facilities to review security, record keeping, reporting and handling prior to issuing a controlled substance registration. The specific security requirements vary by the type of business activity and the schedule and quantity of controlled substances handled. The most stringent requirements apply to manufacturers, importers, exporters and distributors of Schedule I and Schedule II substances. Required security measures include restricted access and physical control of controlled substances through storage in approved vaults, safes and cages and through use of alarm systems and surveillance cameras. Once registered, manufacturing facilities must maintain records documenting the manufacture, receipt and inventory and distribution of all controlled substances. Manufacturers must submit periodic reports to the DEA of the distribution of Schedule I and II controlled substances, Schedule III narcotic substances and other designated substances. All DEA registrants (including manufacturers, importers, exporters and distributors) must comply with security, record keeping and reporting requirements such as reporting any controlled substance thefts or significant losses and following appropriate procedures to destroy or dispose of controlled substances. Imports of Schedule I and II controlled substances for commercial purposes are generally restricted to substances not already available from a domestic supplier or where there is not adequate competition among domestic suppliers. In addition to an importer or exporter registration, importers and exporters must obtain a permit for every import or export of a Schedule I and II substance or Schedule III, IV and V narcotic and submit import or export declarations for Schedule III, IV and V non-narcotics. In some cases, Schedule III non-narcotic substances may be subject to the import/export permit requirement, if necessary, to ensure that the United States complies with its obligations under international drug control treaties.

For drugs manufactured in the United States, the DEA establishes annually an aggregate quota for the amount of substances within Schedules I and II that may be manufactured or produced in the United States based on the DEA's estimate of the quantity needed to meet legitimate medical, scientific, research and industrial needs. Each manufacturer must apply for an individual manufacturing quota (e.g., manufacturing API) or procurement quota (e.g., manufacturing dosage forms or packaging), which represents the amount each facility can manufacture in a given quarter or year. The DEA currently has revised its regulations to require applications for quotas on a semi-annual basis. The quotas apply equally to the manufacturing of the active pharmaceutical ingredient and production of dosage forms. The DEA may adjust aggregate production quotas a few times per year. The DEA can also adjust individual manufacturing or procurement quotas based on manufacturer requests. The DEA has substantial discretion in whether or not to make such adjustments for individual companies.

The various states within the United States also maintain separate controlled substance laws and regulations, including licensing, record keeping, security, distribution and dispensing requirements. The state laws and regulations classify controlled substances into certain schedules, similar to federal law and regulations. Drugs scheduled or rescheduled at the federal level must also be independently scheduled at the state level before they can be commercially marketed. State authorities, including boards of pharmacy, regulate use of controlled substances in each state.

Failure to maintain compliance with applicable requirements, particularly as manifested in the loss or diversion of controlled substances, can result in enforcement action that could have a material adverse effect on our business, operations and financial condition. The DEA, and potentially some state agencies, may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal prosecution.

The United States and the majority of countries are signatories to the UN international drug control treaties which dictate certain scheduling, licensing, restrictions and other requirements involving controlled substances. Because mebufotenin is classified as a Schedule I controlled substance under the UN Convention on Psychotropic Substances, 1971, most countries maintain laws and regulations comparable to those in the United Stated related to mebufotenin and other controlled substances.

Regulation and Procedures Governing Approval of Medicinal Products in the EU

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can initiate clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU generally follows similar pathways as in the United States, although the approval of a medicinal product in the United States is no guarantee of approval of the same product in the EU, either at all or within the same timescale as approval may be granted in the United States. It entails satisfactory completion of pharmaceutical development, nonclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the medicinal product for each proposed indication. It also requires the submission to relevant competent authorities for clinical trials authorization for a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU or its member states (as well as Iceland, Norway and Liechtenstein). If we fail to comply with applicable requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Clinical Trial Approval

In the EU, an applicant for authorization of a clinical trial must obtain prior approval from the national competent authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the relevant independent ethics committee has issued a favorable opinion in relation to the clinical trial. In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which replaced the previous Clinical Trials Directive 2001/20/EC. It has reshaped the system of approvals for clinical trials in the EU. Specifically, the new legislation, which is directly applicable in all EU member states (meaning that no national implementing legislation in each EU member state is required), aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single-entry point—the Clinical Trials Information System, or CTIS, and strictly defined deadlines for the assessment of clinical trial applications. The Clinical Trials Regulation (EU) No. 536/2014 became applicable on January 31, 2022 and contained a three-year transition period which offered sponsors the possibility to choose whether to submit a new clinical trial application under the Clinical Trials Directive 2001/20/EC or the Clinical Trials Regulation (EU) No 536/2014. If the sponsor opted to submit under the Clinical Trials Directive 2001/20/EC and the clinical trial was still ongoing by the end of the transition period, the sponsor was required to transfer the clinical trial to the CTIS by January 31, 2025. Since January 31, 2023, all new clinical trial applications must be made via the CTIS, and all ongoing clinical trials must be conducted under the Clinical Trials Regulation (EU) No 536/2014.

Marketing Authorization

To obtain a marketing authorization for a product under the EU regulatory system, an applicant must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in EU member states (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states (as well as Iceland, Norway and Liechtenstein). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of TRD. For those products for which the use of the centralized procedure is not mandatory, applicants may elect to use the centralized procedure where either the product contains a new active substance indicated for the treatment of other diseases or where the applicant can show that the product constitutes a significant therapeutic, scientific or technical innovation or for which a centralized process is in the interest of patients at an EU level.

Under the centralized procedure, the Committee for Medicinal Products for Human use, or the CHMP, which is the EMA's committee that is responsible for human medicines, established at the EMA is responsible for conducting the assessment of whether a medicine meets the required quality, safety and efficacy requirements and whether the product has a positive risk/benefit/risk profile. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA is 210 days from the receipt of a valid MAA, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the timeframe of 210 days for assessment will be reduced to 150 days (excluding clock stops), but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

PRIME Scheme

The EMA offers a scheme that is intended to reinforce early dialogue with, and regulatory support from, the EMA in order to stimulate innovation, optimize development and enable accelerated assessment of PRIority MEdicines, or PRIME. It is intended to build upon the scientific advice scheme and accelerated assessment procedure offered by the EMA. The scheme is voluntary and eligibility criteria must be met for a medicine to qualify for PRIME.

The PRIME scheme is open to medicines under development and for which the applicant intends to apply for an initial marketing authorization application through the centralized procedure. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicine will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods or therapy or improving existing ones. Applicants will typically be at the exploratory clinical trial phase of development and will have preliminary clinical evidence in patients to demonstrate the promising activity of the medicine and its potential to address to a significant extent an unmet medical need. In exceptional cases, applicants from the academic sector or SMEs (small and medium sized enterprises) may submit an eligibility request at an earlier stage of development if compelling nonclinical data in a relevant model provide early evidence of promising activity, and first in man studies indicate adequate exposure for the desired pharmacotherapeutic effects and tolerability.

If a medicine is selected for the PRIME scheme, the EMA:

- appoints a rapporteur from the CHMP or from the Committee for Advanced Therapies, or CAT, to provide continuous support and to build up knowledge of the medicine in advance of the filing of a marketing authorization application;
- issues guidance on the applicant's overall development plan and regulatory strategy;
- organizes a kick-off meeting with the rapporteur and experts from relevant EMA committees and working groups;
- provides a dedicated EMA contact person; and
- provides scientific advice at key development milestones, involving additional stakeholders, such as health technology assessment bodies and patients, as needed.

Medicines that are selected for the PRIME scheme are also expected to benefit from the EMA's accelerated assessment procedure at the time of application for marketing authorization. Where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

Pediatric Development

In the EU, companies developing a new medicinal product must agree upon a Pediatric Investigation Plan, or PIP, with the EMA and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies, (i.e., because the relevant disease or condition occurs only in adults). The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP unless a waiver applies or a deferral has been granted, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization on the basis of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six-month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two-year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Regulatory Data Protection in the EU

In the EU, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon grant of a marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No. 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity period. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, nonclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a re-evaluation of the risk benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least nine months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the product on the EU market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

Controlled Drugs Classification

In Ireland, mebufotenin is considered a Schedule 1 drug under the Misuse of Drugs Regulations 2017, as amended. Schedule 1 of the Misuse of Drugs Regulations 2017 lists those drugs to which the most restrictive controls apply: they are considered to have no legitimate or medicinal use and can only be imported, exported, produced, supplied and such like under a license issued by the Irish Health Products Regulatory Authority (HPRA), on behalf of the Department of Health. The position in the member states of the EU is not harmonized. Member states have implemented the relevant UN Conventions (the Single Convention of Narcotic Drugs 1961 and the Convention on Psychotropic Substances 1971) into their national legislation, which has led to differences in how controlled substances are regulated in different countries of the EU. It is therefore important to determine at a national level whether a substance is controlled and to comply with the applicable legal requirements. If we are successful in obtaining a marketing authorization in key EU member states, it is likely that rescheduling of mebufotenin will also be required to enable prescribing. There can be no guarantee that such rescheduling would be successful.

In the UK, where part of our manufacturing process takes place, mebufotenin is considered a Class A drug under the Misuse of Drugs Act 1971, as amended, and as a Schedule 1 drug under the Misuse of Drugs Regulations 2001, as amended. Class A drugs are considered to be the most potentially harmful and have the highest level of control exerted over them under the Misuse of Drugs Act 1971. Similarly, Schedule 1 of the Misuse of Drugs Regulations 2001 lists those drugs to which the most restrictive controls apply: they are considered to have no legitimate or medicinal use and can only be imported, exported, produced and supplied under a license issued by the UK Government's Home Office.

Regulatory Requirements After Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product.

These include compliance with the EU's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. The holder of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

In addition, all new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.

Furthermore, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's cGMP requirements and comparable requirements of other regulatory bodies in the EU, which mandate the methods, facilities and controls used in manufacturing, processing and packing of products to assure their safety and identity.

Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of products, are strictly regulated in the EU under Directive 2001/83/EC, as amended. The advertising of prescription-only medicines to the general public is not permitted in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU Directive 2001/83/EC, as amended, the details and enforcement are governed by regulations in each EU member state (as well as Iceland, Norway and Liechtenstein) and differ from one country to another.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any mebufotenin therapy for which we receive regulatory approval for commercial sale will depend, in part, on the availability of coverage and reimbursement for our products from third-party payors, such as government healthcare programs (e.g., Medicare, Medicaid and TRICARE), managed care providers, private health insurers, health maintenance organizations and other organizations. These third-party payors decide which medications they will pay for and will establish reimbursement levels. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. The availability of coverage and extent of reimbursement by governmental and other third-party payors is essential for most patients to be able to afford treatments such as novel therapies. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS. CMS decides whether and to what extent our products will be covered and reimbursed under Medicare. Although private third-party payors tend to follow Medicare practices, no uniform or consistent policy of coverage and reimbursement for drug products exists among third-party payors. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Our ability to successfully commercialize our product candidates, whether as a single agent or combination therapy, will depend in part on the extent to which coverage and adequate reimbursement for our products and related treatments will be available from third-party payors. Moreover, the process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product, and a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

A decision by a third-party payor not to cover or not to separately reimburse for our medical products or therapies using our products could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. If there is coverage for our product candidates, or therapies using our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States will be available for our current or future product candidates, or for any procedures using such product candidates, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future. Further, if we or our collaborators develop therapies for use with our product candidates, we, or our collaborators, will be required to obtain coverage and reimbursement for these therapies separate and apart from the coverage and reimbursement we seek for our product candidates, once approved.

Further, third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to secure coverage and reimbursement for any product candidate that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of such product, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may, nonetheless, not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product, after approval, as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. We expect to experience pricing pressures from third-party payors in connection with the potential sale of any of our product candidates.

Lastly, in some foreign countries, the proposed pricing for a drug and its reimbursement status must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example:

- in the EU, member states can restrict the range of medicinal products for which their national health insurance systems provide reimbursement and, in most EU countries, the prices of medicinal products for human use must be approved by national health authorities, before they may be supplied;

- a common criterion relied upon by almost all EU Member States for pricing decisions is international reference pricing (the methodology and weight to be attached varies between countries);

- reimbursement decisions in EU/EEA are typically based on various forms of health technology assessment, including cost effectiveness determinations. From 2025, the EU's Health Technology Assessment Regulation (Regulation (EU) 2021/2282), or HTA Regulation, will start to come into effect providing for a common assessment of clinical effectiveness to be taken into account by national reimbursement authorities across EU/EEA; and

- additional public procurement tenders are widely used for purchasing of medicinal products by hospitals.

The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel trade (arbitrage between low-priced and high-priced member states) can further reduce prices. Acceptance of any medicinal product for reimbursement may come with cost, use and often volume restrictions, which again can vary by country. In addition, results-based rules of reimbursement may apply.

Notwithstanding any of the above, as a Schedule I substance under the CSA, mebufotenin is currently deemed to have no accepted medical use and therapies that use mebufotenin are currently precluded from reimbursement in the United States.

Other Healthcare Laws and Compliance Requirements

Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable federal and state fraud and abuse laws, as well as other healthcare laws and regulations. These laws may impact, among other things, our business or financial arrangements and relationships through which we research, as well as market, sell and distribute the product candidates for which we obtain approval. In addition, we may be subject to health information privacy regulation by both the federal government and the United States in which we conduct our business. In the United States, the laws that may affect our ability to operate include, among others:

- The federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare and Medicaid. The term "remuneration" has been interpreted broadly to include anything of value. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the federal Anti-Kickback Statute is violated. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between manufacturers on one hand and prescribers, purchasers and formulary managers on the other. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but the exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor;

- The federal civil and criminal false claims laws, such as the FCA, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other third-party payors, that are false, fictitious or fraudulent; from knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit property to the federal government; or from knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. A claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the FCA. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring qui tam actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- The federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transferring of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular provider, practitioner or supplier of items or services reimbursable by a federal or state healthcare program;

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including both public and private third-party payors, or to obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (i.e., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statements or representations, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statements or entry in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its respective implementing regulations, which imposes, among other things, certain requirements on covered entities, including certain covered healthcare providers, health plans and healthcare clearinghouses and their respective business associates relating to the privacy, security and transmission of individually identifiable health information as well as their covered subcontractors. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, those independent contractors or agents of covered entities that create, receive, maintain, transmit or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions;

- The federal Physician Payment Sunshine Act, created under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, or the ACA, which requires applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services, or HHS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician providers, including physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, certified nurse midwives and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;

- Federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- Analogous state and foreign equivalents of each of the healthcare laws and regulations described above, such as anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state and local marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements; state laws that require pharmaceutical companies to comply with the pharmaceutical industry voluntary compliance guidelines and other relevant compliance guidance promulgated by the federal government, such as the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals; state laws that require the reporting of information related to drug pricing; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; state and local laws that require the licensure and/or registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information that may be more stringent than those in the United States (such as the EU, which adopted the GDPR), many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The full scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have continued to increase their scrutiny on interactions between healthcare companies and healthcare providers, which has led to a number of significant investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including our arrangements with physicians and other healthcare providers and entities, such as our Centers of Excellence or therapists, are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs (such as Medicare and Medicaid), imprisonment and additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our Centers of Excellence and therapists, are found to be not in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions.

Ensuring that our current and future business arrangements with third parties, and our business generally, comply with applicable healthcare laws and regulations, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

Other Healthcare Laws and Compliance Requirements outside the United States

Outside of the United States, individual countries impose a variety of anti-corruption laws, most notable of which is the UK Bribery Act 2010 because of its apparent extra-territorial effect. Within the EU, our operations will be subject to anti-corruption laws in most member states. There is a heightened risk both from application of the FCPA and from national laws in many European and other countries because many of their healthcare professionals are categorized as government officials. These laws will impose a variety of strictures on our business which are time consuming and expensive, including limiting engagements with healthcare professionals, the requirement to obtain prior authorizations for promotional activities from employers and/or government or industry bodies, and the requirement to supply transparency information regarding the interactions. Failure to comply with these laws is potentially very costly and can lead to reputational damage, fines, penalties and imprisonment as well as investigations and additional oversight of our business activities.

Regulations Governing the Use, Processing and Cross-border Transfer of Personal Information

In the event we decide to conduct future clinical trials in Europe, the United States or other jurisdictions, we may be subject to additional privacy and data protection requirements and restrictions. The collection, use, storage, disclosure, transfer or other processing of personal data regarding individuals in the EEA, including personal health data, is subject to EU and national level data protection and privacy laws including, most notably, the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on entities that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates in certain circumstances, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches and taking certain measures when engaging third-party processors that will have access to personal data. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States. Entities that fail to comply with the requirements of the GDPR may be subject to very significant penalties, including potential fines of up to the greater of €20 million or 4% of annual global revenue. The GDPR increases our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR is a rigorous, costly and time-intensive process that increases our cost of doing business and requires us to put in place specific business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation and reputational harm in connection with our European personal data processing activities.

In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health and personal information privacy laws, and federal and state consumer protection laws, govern the collection, use, processing, storage, transmission, disclosure, destruction and protection of health-related and other personal information. For example, the California Consumer Privacy Act of 2018, or CCPA, became effective on January 1, 2020, and created new individual privacy rights for California consumers and placed increased privacy and security obligations on entities handling certain personal data of California consumers. The CCPA requires companies subject to the legislation to provide new disclosure to consumers about such companies' data collection, use and sharing practices and provide such consumers new ways to opt-out of certain sales or transfers of personal information. The CCPA provides for civil penalties as well as a private right of action for certain data breaches that result in the loss of personal information. This private right of action may increase the likelihood of, and risks associated with, data breach litigation. In addition, the California Privacy Rights Act of 2020, or CPRA, went into effect on January 1, 2023. The CPRA, among other things, gives California residents the ability to limit the use of their personal information, further restricts the use of cross-contextual advertising, establishes restrictions on the retention of personal information, expands the types of data breaches subject to the CCPA's private right of action and establishes a new California Privacy Protection Agency to implement and enforce the CCPA and CPRA. Other states and the U.S. federal government are considering comprehensive privacy laws, and on January 1, 2023, the Virginia Consumer Data Protection Act became effective, which contains provisions that require businesses subject to the legislation to conduct data protection assessments in certain circumstances and that require opt-in consent from Virginia consumers to process certain sensitive personal information. In addition, Colorado enacted the Colorado Privacy Act, and Connecticut enacted the Connecticut Data Privacy Act, each of which took effect on July 1, 2023, and Utah enacted the Consumer Privacy Act, which became effective on December 31, 2023. Several other states, including New Hampshire, Delaware, Nebraska, Nevada and Oklahoma have also enacted privacy laws that have recently taken effect. Moreover, laws in all 50 U.S. states require businesses to provide notice to consumers whose personal information has been disclosed as a result of a data breach. These state laws, and such other proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies.

The regulatory framework for data privacy and security issues in the United States and abroad is rapidly evolving and likely to remain uncertain for the foreseeable future. Compliance with applicable U.S. and foreign privacy and data protection laws and regulations is a rigorous and time-intensive process and could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose certain data, or in some cases, impact our ability to operate in certain jurisdictions.

Healthcare Reform

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs pharmaceutical costs. This has resulted in several presidential executive orders, Congressional inquiries, and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, control the costs of drugs, including under Medicare and Medicaid, restrict reimbursement, require the substitution of generic products for branded prescription drugs, and reform government program reimbursement methodologies for drug products. For example, under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs was eliminated. Elimination of this cap has, in some cases, required pharmaceutical manufacturers to pay more in rebates than they received on the sale of products. Further, the Infrastructure Investment and Jobs Act added a requirement, effective January 1, 2023, for manufacturers of certain single-source drugs (including biologics and biosimilars) separately paid for under Medicare Part B for at least 18 months and marketed in single-dose containers or packages (known as refundable single-dose containers or single-use package drugs) to provide annual refunds for any portions of the dispensed drug that are unused and discarded if those unused or discarded portions exceed an applicable percentage defined by statute or regulation. Manufacturers are subject to periodic audits and those that fail to pay refunds for their refundable single-dose containers or single-use package drugs shall be subject to civil monetary penalties. There have also been and continue to be a number of other initiatives at the United States federal and state levels that seek to reduce healthcare costs, including the Budget Control Act which, subject to certain temporary suspension periods, imposed 2% reductions in Medicare payments to providers per fiscal year starting April 1, 2013, and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, unless additional Congressional action is taken. Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices.

Several healthcare reform proposals culminated in the enactment of Inflation Reduction Act, or IRA, which, among other things, requires HHS to directly negotiate the selling price of a statutorily specified number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. The negotiated price may not exceed a statutory ceiling price. Only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for single-source biologics) are eligible to be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. For 2026, the first year in which negotiated prices become effective, CMS selected 10 high-cost Medicare Part D products in 2023, negotiations began in 2024, and the negotiated maximum fair price for each product has been announced. In addition, CMS selected and announced the negotiated maximum fair price for 15 additional Medicare Part D drugs, which will become effective in 2027. For 2028, CMS selected an additional 15 drugs, comprised of drugs covered under Medicare Part D and, for the first time, drugs payable under Medicare Part B. For 2029 and subsequent years, 20 Part B or Part D drugs will be selected. Currently, a drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA's price negotiation requirements, but will lose that exclusion if it receives designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. However, as a result of a statutory amendment enacted in July 2025, beginning with the 2028 negotiated price applicability year, a drug may be designated for more than one rare disease or condition and still be excluded from price negotiation, as long as the only approved indications are for such rare diseases or conditions. The IRA also imposes rebates on Medicare Part D and Part B drugs whose prices have increased at a rate greater than the rate of inflation, and in November 2024, CMS finalized regulations for the Medicare Part B and Part D inflation rebates. The IRA also eliminated, beginning in 2025, the coverage gap under Medicare Part D by significantly lowering the enrollee maximum out-of-pocket cost and requiring manufacturers, in order for their drugs to be reimbursed by Medicare Part D, to subsidize, through a newly established manufacturer discount program, 10% of Part D enrollees' prescription costs for brand drugs below the out-of-pocket limit, and 20% once the out-of-pocket limit has been reached. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including significant civil monetary penalties. These provisions may be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers. Thus, while it is unclear how the IRA will be implemented, it will likely have a significant impact on the biopharmaceutical industry and the pricing of prescription drug products. It is unclear to what extent other statutory, regulatory, and administrative initiatives will be enacted and implemented in the future.

In May 2025, the administration published an executive order regarding most favored nation, or MFN, drug pricing, which is sometimes referred to as international reference pricing. This executive order directs the Secretary of HHS to communicate MFN price targets to pharmaceutical manufacturers, and if significant progress towards MFN pricing is not delivered, to propose a rulemaking plan to implement MFN pricing. Recently, on December 23, 2025, CMS issued proposed regulations to establish, under the Center for Medicare and Medicaid Innovation, two mandatory MFN demonstration models under Medicare Parts B and D, respectively. If these rules or other MFN pricing rules are finalized, they are likely to mandate reduced prices of at least some drugs in the United States, if they are also sold in comparator countries.

At the state level in the United States, legislatures are increasingly enacting laws and implementing regulations designed to control pharmaceutical and biologic product pricing, including price constraints, restrictions on certain product access, reporting on price increases and the introduction of high-cost drugs. In some states, laws have been enacted to encourage importation of lower cost drugs from other countries and bulk purchasing. For example, the FDA released a final rule in September 2020 providing guidance for states to build and submit importation plans for certain prescription drugs from Canada into the United States, and FDA authorized the first such plan in Florida in January 2024. This plan has been granted extensions until May 6, 2026.

Employees

As of December 31, 2025, we employed seventy-three people. Of our workforce, fifty-six employees are engaged in research and development activities with the rest providing administrative, business and operations support.

None of our employees are represented by labor unions or covered by collective bargaining agreements. We have not experienced any employee litigation or claims and consider our employee relations to be good.

C. Organizational Structure

As of December 31, 2025, we had one subsidiary. The following table sets out for our principal subsidiary, the country of incorporation, and the percentage ownership and voting interest held by us.

Company	Country of Incorporation	Percentage Ownership and Voting Interest	Main Activities
GH Research Ireland Limited	Ireland	100%	Clinical operations and research and development

D. Property, Plants and Equipment

Facilities

We lease a facility of 391 square meters of office space, located at Joshua Dawson House, Dawson Street, Dublin 2, Ireland and a facility of 35 square meters of office space, located at 28 Baggot Street Lower, Dublin 2, Ireland. We believe our facilities are adequate for our current needs, including our short-term needs, and that suitable additional or substitute space would be available in Dublin, if needed.

We are not aware of any environmental issues or other constraints that would materially impact the intended use of our facility.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion and analysis of our financial condition and results of operations together with our audited consolidated financial statements, including the notes thereto, included in this Annual Report.

Our audited consolidated financial statements were prepared in accordance with IFRS. None of our financial statements was prepared in accordance with U.S. GAAP. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business and our expectations with respect to liquidity and capital resources, includes forward-looking statements. These forward-looking statements are subject to numerous risks and uncertainties, including, but not limited to, those risks and uncertainties described in "Cautionary Statement Regarding Forward-Looking Statements," "Item 3. Key Information—D. Risk Factors" and elsewhere in this Annual Report.

A. Operating Results

Overview

We are a clinical-stage biopharmaceutical company dedicated to transforming the lives of patients by developing a practice-changing treatment in depression. Our initial focus is on developing our novel and proprietary mebufotenin therapies for the treatment of patients with treatment-resistant depression, or TRD.

Our portfolio currently includes GH001, our proprietary inhalable mebufotenin product candidate and GH002, our proprietary intravenous mebufotenin product candidate. While GH001 is currently delivered via a vaporization device produced by a third party, we are developing a proprietary aerosol delivery device, which is currently in clinical investigation in Europe. We have completed two Phase 1 healthy volunteer clinical trials for GH001 (GH001-HV-101 and GH001-HV-103), in which administration of GH001 via inhalation was observed to be well tolerated at the investigated single dose levels and in an individualized dosing regimen, or IDR, with intra-subject dose escalation within a single day. We have also completed a Phase 1/2 clinical trial in patients with TRD (GH001-TRD-102) and a multi-center, randomized, double-blind, placebo-controlled Phase 2b trial with an Open-Label Extension of GH001 in patients with TRD (GH001-TRD-201). Based on observed clinical activity in these clinical trials, we believe that administration of GH001 has the potential to induce ultra-rapid remissions as measured by the Montgomery–Åsberg Depression Rating Scale, or MADRS, in TRD patients.

We have incurred losses since inception, including net losses of $48.3 million, $39.0 million and $35.6 million for the years ended December 31, 2025, 2024 and 2023, respectively. As of December 31, 2025, we had an accumulated deficit of $154.4 million, compared to an accumulated deficit as of December 31, 2024, of $106.4 million. We expect to incur significant expenses and operating losses for the foreseeable future as we expand our research and development activities. In addition, our losses from operations may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials, our expenditures on other research and development activities and based on foreign currency translation differences. We anticipate that our expenses will increase significantly in connection with our ongoing activities, if and as we:

- continue to develop and conduct clinical trials, including in expanded geographies such as the United States, for our GH001 and GH002 product candidates for our initial indications and any additional indications;
- continue both the technical development and expansion of our external manufacturing capabilities for our current product candidates GH001 and GH002 and of the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001;
- initiate and continue research and development, including technical, nonclinical, clinical, and discovery efforts for any future product candidates;
- seek to identify additional product candidates;
- seek regulatory approvals for our product candidates GH001 and GH002 including the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001, or any other product candidates that successfully complete clinical development;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate and device development and help us comply with our obligations as a public company;
- hire and retain additional personnel, such as clinical, quality control, scientific, commercial, sales, marketing and administrative personnel;
- continue to prepare, file, prosecute, maintain, protect and enforce our intellectual property rights and claims;
- establish sales, marketing, distribution, manufacturing, supply chain and other commercial infrastructure in the future to commercialize various products for which we may obtain regulatory approval;
- comply with ongoing regulatory requirements for products approved for commercial sale, if ever;
- acquire or in-license other product candidates, medical devices to deliver our product candidates, and other technologies; and
- incur increased costs as a result of operating as a public company.

In addition, as we progress toward marketing approval for any of our product candidates, we also expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of one or more of our product candidates or other research and development initiatives, which could have a material adverse effect on our business, results of operations, and financial condition. We will need to generate significant revenue to achieve profitability, and we may never do so.

We are subject to a number of risks comparable to those of other similar companies, including dependence on key individuals; the need to develop product candidates with the required safety and efficacy profile and which support regulatory approval and are commercially viable; competition from other companies, many of which are larger and better capitalized; and the need to obtain adequate additional financing to fund the development of our product candidates.

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $280.7 million, compared to cash, cash equivalents, other financial assets and marketable securities of $182.6 million as of December 31, 2024. We believe that our existing cash, cash equivalents and marketable securities will be sufficient for us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—B. Liquidity and Capital Resources" below.

Financial Operations Overview

Revenue

We have not generated any revenue since inception and do not expect to generate any revenue from the sale of products for several years, if at all. If our development efforts for our current or future product candidates are successful and result in regulatory approval or collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements that we may enter into with third parties. Because of the numerous risks and uncertainties associated with product development, regulatory approval and market acceptance, we are unable to predict the amount or timing of product revenue.

Operating Expenses

Research and Development Expenses

Research and development expenses primarily represent costs incurred by us for the following:

- development costs, including expenses incurred under agreements with third parties, such as consultants, investigational sites and CROs, that conduct our nonclinical studies and clinical trials and other scientific development services;
- costs to develop our manufacturing technology and infrastructure, including costs incurred with third-party CMOs to acquire, develop and manufacture drug substance, drug product, and delivery device materials for nonclinical studies and clinical trials;
- costs incurred to maintain compliance with regulatory requirements; and
- other expenses, including costs of outside consultants, insurance and other operating costs.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as other current assets or other current liabilities.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials and related product manufacturing expenses. As a result, we expect that our research and development expenses will continue to increase over the next several years as we: (i) advance the clinical development of GH001 for TRD; (ii) advance the clinical development of GH001 for BDII and a current depressive episode and PPD; (iii) advance GH002 and any potential future product candidate into clinical development; and (iv) build our third-party or in-house process development, analytical, manufacturing and related capabilities, increase personnel costs and prepare for regulatory filings related to our potential or future product candidates. We also expect to incur additional IP-related expenses as we file further patent applications and prosecute our intellectual property to protect innovations arising from our research and development activities.

The successful development and commercialization of GH001 and GH002 and any potential future product candidate is highly uncertain. This is due to the numerous risks and uncertainties associated with development and commercialization, including the following:

- successful enrollment in and completion of clinical trials;
- successful completion of nonclinical studies;
- sufficiency of our financial and other resources to complete the necessary technical development work, nonclinical studies and clinical trials;
- receiving regulatory approvals or clearance for conducting our planned clinical trials or future clinical trials;
- receiving positive data from our clinical trials that support an acceptable risk-benefit profile of GH001 and GH002 and any future product candidates in the intended populations;
- receipt and maintenance of regulatory and marketing approvals from applicable regulatory authorities;
- establishing and scaling up, through third-party manufacturers, manufacturing capabilities of clinical supply for our clinical trials and commercial manufacturing, if any product candidates are approved;
- entry into collaborations to further the development of GH001 and GH002 and any future product candidates, including any required medical devices;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for GH001 and GH002 and any future product candidates;
- successfully launching commercial sales of GH001 and GH002 and any future product candidates, if approved;
- acceptance of our current and future product candidates' benefits and uses, if approved, by patients, the medical community and third-party payors; and
- maintaining a continued acceptable safety profile of GH001 and GH002 and our future product candidates following approval.

A change in the outcome of any of these variables with respect to the development of our product candidates in nonclinical and clinical development could mean a significant change in the costs and timing associated with their development. For example, if we are required by the FDA, or other comparable foreign regulatory authorities, to perform clinical trials in addition to those that we currently expect, or if there are any delays in establishing appropriate manufacturing arrangements for our product candidates or for the medical devices required to deliver our product candidates, or if there are any delays in completing our clinical trials or the development of any of our product candidates or of the medical devices required to deliver our product candidates.

Our research and development expenses may vary substantially from period to period based on the timing of our research and development activities, including due to timing of initiation of clinical trials and enrollment of patients in clinical trials. Research and development expenses are expected to increase as we advance the clinical development of our inhalable mebufotenin product candidate GH001, and further advance the research and development of our intravenous mebufotenin product candidate GH002 and any future product candidates. The successful development of our product candidates is highly uncertain.

General and Administrative Expenses

General and administrative expenses consist primarily of:

- professional fees, including consulting, accounting, legal, tax and audit services;
- personnel expenses, including salaries and related expenses; and
- other expenses, including expenses for rent and maintenance of facilities, insurance and other operating costs.

We anticipate that our general and administrative expenses will continue to increase in the future as we further increase our headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. In addition, we have incurred and expect to continue to incur increased expenses associated with being a public company, including increased costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs, investor and public relations costs and costs associated with other administrative and professional services.

Net Finance Income

Net finance income consists of:

- interest income on cash and cash equivalents, other financial assets and marketable securities;
- interest expense;
- the net gain or loss on cash equivalents classified at fair value through profit and loss, or FVTPL; and
- expected credit losses relating to investments in marketable securities.

Foreign Exchange Gain/Loss

Foreign exchange gains/losses consist of foreign exchange impacts arising from foreign currency transactions.

Taxation

We are subject to corporate taxation in Ireland. Due to the nature of our business, we have generated losses since inception and have therefore not paid Irish corporation tax.

Unused tax losses can be carried forward indefinitely against future trading income. As there is no certainty that we will generate sufficient taxable profits to be able to utilize these tax loss carry-forwards in full, we have concluded not to recognize any deferred tax assets at December 31, 2025 or 2024.

Results of Operations

Comparison of the Years Ended December 31, 2025 and 2024

The following table summarizes our results of operations for the years ended December 31, 2025 and 2024:

	Year Ended December 31,		
	2025	2024	Change
	(in USD thousands)		
Operating Expenses:			
Research and development	(38,765)	(35,016)	(3,749)
General and administrative	(21,953)	(15,296)	(6,657)
Loss from operations	**(60,718)**	**(50,312)**	**(10,406)**
Net finance income[1]	10,707	9,222	1,485
Foreign exchange gain	1,753	2,129	(376)
Loss for the year	**(48,258)**	**(38,961)**	**(9,297)**

[1] Net finance income for the years ended December 31, 2025 and 2024, comprises finance income, finance expense and expected credit losses.

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2025 and 2024:

	Year Ended December 31,		
	2025	2024	Change
	(in USD thousands)		
External research and development expenses[1]	(26,178)	(27,800)	1,622
Employee expenses[2]	(12,587)	(7,216)	(5,371)
Research and development	**(38,765)**	**(35,016)**	**(3,749)**

[1] Includes depreciation expense.

[2] Includes share-based compensation expense of $3.9 million and $0.5 million for the years ended December 31, 2025 and 2024, respectively.

The following table summarizes our research and development expenses for our product candidates for the years ended December 31, 2025 and 2024:

	Year Ended December 31,		
	(in USD thousands)		
	2025	2024	Change
GH001	(25,490)	(24,645)	(845)
GH002	(2,502)	(1,748)	(754)
GH003	—	(18)	18
Related to multiple product candidates and exploratory work for potential future product candidates	(10,773)	(8,605)	(2,168)
Research and development	**(38,765)**	**(35,016)**	**(3,749)**

Research and development expenses increased by $3.7 million to $38.8 million for the year ended December 31, 2025, from $35.0 million for the year ended December 31, 2024. The increase is primarily due to increased expenses relating to technical development activities, nonclinical activities and employee expenses, which included an increase in share-based compensation expense due to the timing of share option grants year on year. These increases have been partly offset by a decrease in clinical development expenses including clinical trial expenses and an increase in the benefit of a research and development tax credit.

Research and development expenses for our product candidates will fluctuate from year to year primarily due to the nature and timing associated with the various lifecycle stages of each candidate.

Research and development expenses relating to GH001 increased by $0.8 million in the year ended December 31, 2025, primarily due to an increase in technical development activities and nonclinical activities, partly offset by a decrease in clinical development activities including clinical trial expenses.

Research and development expenses relating to GH002 increased by $0.8 million in the year ended December 31, 2025, primarily due to an increase in nonclinical activities, partly offset by a decrease in technical development expenses.

Research and development expenses which relate to multiple product candidates increased by $2.2 million in the year ended December 31, 2025, primarily due to an increase in employee expenses, partly offset by a decrease in technical development expenses, clinical development expenses and an increase in the benefit of a research and development tax credit.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2025 and 2024:

	Year Ended December 31,		
	2025	**2024**	**Change**
		(in USD thousands)	
External costs	(12,956)	(10,182)	(2,774)
Employee expenses[(1)]	(8,695)	(4,820)	(3,875)
Depreciation	(302)	(294)	(8)
General and administrative	**(21,953)**	**(15,296)**	**(6,657)**

[(1)]Includes share-based compensation expense of $4.6 million and $0.7 million for the years ended December 31, 2025 and 2024, respectively.

General and administrative expenses increased by $6.7 million to $22.0 million for the year ended December 31, 2025, from $15.3 million for the year ended December 31, 2024. The increase is primarily due to an increase in professional fees and employee expenses, which included an increase in share-based compensation expense due to the timing of share option grants year on year, in our general and administrative functions to support our growth initiatives.

Net Finance Income

Our net finance income increased by $1.5 million to $10.7 million for the year ended December 31, 2025, from $9.2 million for the year ended December 31, 2024. The increase is primarily due to an increase in finance income relating to return on investments.

Foreign Exchange Gain

Foreign exchange gain is $1.8 million for the year ended December 31, 2025, a decrease of $0.4 million from a gain of $2.1 million for the year ended December 31, 2024. This movement is primarily as a result of the translation of our assets and liabilities from their denominated currencies into the functional currency of each entity.

Comparison of the Years Ended December 31, 2024 and 2023

For a discussion of our statements of operations for the years ended December 31, 2024 and 2023, see the section "Item 5. Operating and Financial Review and Prospects—A. Operating Results—Results of Operations—Comparison of the Years Ended December 31, 2024 and 2023" in our Annual Report on Form 20-F/A for the year ended December 31, 2024.

B. Liquidity and Capital Resources

Sources of Liquidity

We have incurred operating losses since inception, and we have not generated any revenue from any product sales or any other sources. We have not yet commercialized any of our product candidates, which are in various phases of technical and clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. We have funded our operations to date primarily through equity financings, including our initial public offering. In February 2025, we completed a public offering in which we issued and sold 10,000,000 ordinary shares at $15.00 per share. The net proceeds of the offering were $139.8 million, after deducting underwriting discounts and directly attributable transaction costs of $10.2 million.

As of December 31, 2025 we had cash, cash equivalents and marketable securities of $280.7 million, compared to cash, cash equivalents, other financial assets and marketable securities of $182.6 million as of December 31, 2024.

We plan to continue to fund our operating and capital funding needs through sales of additional equity or other forms of financing. We may also consider pursuing strategic partnerships for clinical development and commercialization of our product candidates. The sale of additional equity would result in dilution to our shareholders.

For a discussion of our sources of liquidity for the year ended December 31, 2023, see the section "Item 5. Operating and Financial Review and Prospects—B. Liquidity and Capital Resources—Sources of Liquidity" in our Annual Report on Form 20-F/A for the year ended December 31, 2024.

Cash Flows

Comparison of the Years Ended December 31, 2025 and 2024

The following table summarizes our cash flows for the years ended December 31, 2025 and 2024:

	Year Ended December 31,		
	2025	**2024**	**Change**
	(in USD thousands)		
Net cash used in:			
Net cash flows used in operating activities	(43,552)	(42,285)	(1,267)
Net cash flows from investing activities	46,172	65,135	(18,963)
Net cash flows from/(used in) financing activities	139,651	(304)	139,955
Net increase in cash and cash equivalents	**142,271**	**22,546**	**119,725**

Net Cash Flows Used in Operating Activities

Net cash flows used in operating activities increased by $1.3 million to $43.6 million for the year ended December 31, 2025, from $42.3 million for the year ended December 31, 2024, due to an increase in loss from operations for the period and movement in working capital.

Net Cash Flows From Investing Activities

Net cash flows from investing activities decreased by $19.0 million to $46.2 million for the year ended December 31, 2025, from $65.1 million for the year ended December 31, 2024, primarily due to a decrease in the proceeds from the sale of other financial assets.

Net Cash Flows From/(Used in) Financing Activities

Net cash flows from financing activities increased to $139.7 million in the year ended December 31, 2025, from net cash flows used in financing activities of $0.3 million for the year ended December 31, 2024. The increase is due to the receipt of proceeds from the public offering which took place during the year ended December 31, 2025.

Comparison of the Years Ended December 31, 2024 and 2023

For a discussion of our cash flows for the years ended December 31, 2024 and 2023, see the section "Item 5. Operating and Financial Review and Prospects—B. Liquidity and Capital Resources—Cash Flows—Comparison of the Years Ended December 31, 2024 and 2023" in our Annual Report on Form 20-F/A for the year ended December 31, 2024.

Funding Requirements

We expect our expenses to continue to increase substantially in connection with our ongoing research and development activities, particularly as we advance the technical development work, nonclinical studies and clinical trials of our product candidates and the medical devices required to deliver such product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution. Furthermore, we have incurred and expect to continue to incur additional costs associated with operating as a public company. We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials, including in expanded geographies such as the United States, for our GH001 and GH002 product candidates for our initial indications and any additional indications;
- continue both the technical development and expansion of our external manufacturing capabilities for our current product candidates GH001 and GH002 and of the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001;
- initiate and continue research and development, including technical, nonclinical, clinical, and discovery efforts for any future product candidates;
- seek to identify additional product candidates;
- seek regulatory approvals for our product candidates GH001 and GH002 including the medical devices required to deliver these product candidates, such as our proprietary aerosol delivery device for GH001, or any other product candidates that successfully complete clinical development;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate and device development and help us comply with our obligations as a public company;
- hire and retain additional personnel, such as clinical, quality control, scientific, commercial, sales, marketing and administrative personnel;
- continue to prepare, file, prosecute, maintain, protect and enforce our intellectual property rights and claims;

- establish sales, marketing, distribution, manufacturing, supply chain and other commercial infrastructure in the future to commercialize various products for which we may obtain regulatory approval;
- comply with ongoing regulatory requirements for products approved for commercial sale, if ever;
- acquire or in-license other product candidates, medical devices to deliver our product candidates, and other technologies; and
- incur increased costs as a result of operating as a public company.

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $280.7 million, compared to cash, cash equivalents, other financial assets and marketable securities of $182.6 million as of December 31, 2024. We believe that our existing cash, cash equivalents and marketable securities will be sufficient for us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. However, we have based this estimate on assumptions that may prove to be wrong and we could exhaust our capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with product development, we may incorrectly estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our present and future funding requirements and timing and amount of our operating expenditures, both in the near- and long-term, depend on many factors, including, but not limited to:

- the scope, progress, results and costs of researching and developing our GH001 and GH002 product candidates, additional mebufotenin delivery approaches and the medical devices required to deliver these therapies for our initial and any additional indications, as well as other product candidates we may develop;
- the timing and uncertainty of, and the costs involved in, obtaining marketing approvals for our GH001 and GH002 product candidates including the medical devices required to deliver these therapies for our initial and any additional indications, and other product candidates we may develop and pursue;
- the number of future product candidates that we may pursue and their development requirements;
- the number of jurisdictions in which we plan to seek regulatory approvals;
- if approved, the costs of commercialization activities for GH001 and GH002 for any approved indications, or any other product candidate that receives regulatory approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution, and manufacturing capabilities;
- subject to receipt of regulatory approval, revenue, if any, received from commercial sales of GH001 and GH002 and the respective medical devices for any approved indications or any other product candidates;
- the extent to which we may in-license or acquire rights to other products, product candidates, medical devices or technologies;
- our headcount growth and associated costs as we expand our research and development, increase our office space, and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications and maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property-related claims;
- the effect of competing product and market developments; and
- the ongoing costs of operating as a public company.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, convertible debt financings, strategic collaborations and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our existing shareholders may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of such existing shareholders. Debt financing, if available, may result in fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through collaborations or marketing, distribution, licensing and royalty arrangements with third parties, we may have to relinquish valuable rights to our intellectual property or technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us or issue and sell our shares, which may result in dilution to our shareholders. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

For more information as to the risks associated with our future funding needs, see "Item 3. Key Information—D. Risk Factors".

C. Research and Development, Patents and Licenses, etc.

See "Item 4. Information on the Company—B. Business Overview" and "Item 5. Operating and Financial Review and Prospects—A. Operating Results—Financial Operations Overview."

D. Trend Information

Other than as disclosed elsewhere in this Annual Report, we are not aware of any trends, uncertainties, demands, commitments or events since December 31, 2025, that are reasonably likely to have a material adverse effect on our liquidity or capital resources, or that would cause the reported financial information in this Annual Report to not be necessarily indicative of future operating results or financial conditions.

E. Critical Accounting Estimates

See Note 2 in the notes to our consolidated financial statements appearing elsewhere in this Annual Report for a description of critical accounting estimates.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management

The following table presents information about our current executive officers and directors. The term of each of our directors is one year and, accordingly, will expire at our annual general meeting of shareholders to be held in 2026. Ages are as of December 31, 2025.

Name	Position(s)	Age
Executive Officers		
Velichka Valcheva	Chief Executive Officer	51
Magnus Halle	Managing Director, Ireland	29
Julie Ryan	Vice President, Finance	40
Aaron Cameron	Chief Operating Officer	41
Non-Executive Directors		
Florian Schönharting	Chairman of the Board of Directors	57
Michael Forer	Vice Chairman of the Board of Directors	60
Dermot Hanley	Director	61
Duncan Moore	Director	66

Unless otherwise indicated, the current business address for our executive officers and our non-executive directors is GH Research PLC, Joshua Dawson House, Dawson Street, Dublin 2, D02 RY95, Ireland.

Executive Officers

Velichka (Villy) Valcheva, MD, MSc, has served as our Chief Executive Officer since September 2024. Prior to this, Dr. Valcheva served as our Chief Medical Officer since February 2024 and Vice President of Clinical Research and Medical Affairs since August 2023. Dr. Valcheva has more than 20 years of experience in various leadership roles in pharmaceutical and biotech industries. Dr. Valcheva served as VP and Head of Medical Affairs International for Albireo from 2020 until 2023, as well as Medical Lead/Monitor FIH study and clinical development from 2022. Prior to this, Dr. Valcheva served as Global Senior Medical Director Oncology - Hepatocellular Carcinoma for Ipsen from 2018 to 2020. Dr. Valcheva holds a Masters in Pharmaceutical Medicine from Trinity College Dublin, Ireland, as well as a Dr. Med. from University of Medicine – Plovdiv, Bulgaria.

Magnus Halle, has served as our Managing Director, Ireland since November 2020, is one of our co-founders, and served as a consultant to us from our founding in 2018 to 2020. Previously, Mr. Halle served as Analyst at NB Capital ApS, a position he held from 2018 to 2021. Additionally, from 2019, he served as the Money Laundering Reporting Officer at NB Capital ApS. Prior to that, from 2016 to 2018, he was the Personal Assistant to Florian Schönharting at NB Capital ApS. Mr. Halle holds a BSc in Economics and Business Administration from Copenhagen Business School.

Julie Ryan, FCA, has served as our Vice President, Finance since January 2021. Previously, Ms. Ryan has served in a number of senior finance roles including Ardagh Group plc, where she was Group Reporting Manager from 2018 to 2020, Sherry FitzGerald, where she was Commercial Business Partner in 2018, ICON plc, where she was Assistant Manager, Commercial/Finance Business Partnering from 2015 to 2018 and Brambles Ltd, where she was Finance Manager from 2013 to 2015. Ms. Ryan qualified as a chartered accountant with PricewaterhouseCoopers and holds a B.Comm (Acc) from University College Dublin and a MAcc from University College Dublin's Michael Smurfit Graduate Business School.

Aaron Cameron, has served as our Chief Operating Officer since January 2024. Prior to this, he served as our Vice President, Technical Development since August 2021, before taking the role of Vice President, Technical Development and Operational Planning in December 2022. Previously Mr. Cameron has served in a number of senior technical, supply chain and program management positions including Viatris, where he was Head of Device Program Management from 2020 to 2021, and Iterum Therapeutics, where he held roles as VP, Supply Chain and Logistics and Director of Drug Product Development and Manufacturing, between 2016 and 2021. From 2013 to 2016, Mr. Cameron served in a variety of roles in R&D in Mylan, after serving in a variety of roles in R&D, Commercialization and Manufacturing in MSD between 2006 and 2012. Mr. Cameron holds a B.Sc. in Chemical and Pharmaceutical Sciences from Dublin City University, a M.Sc. in Industrial Pharmaceutical Science from the Royal College of Surgeons, Dublin, and an MBA from Bradford University.

Non-Executive Directors

Florian Schönharting, has served as the Chairman of our Board of Directors since 2018. Mr. Schönharting is one of our co-founders. Mr. Schönharting is also co-founder of Forward Pharma A/S, served on its board of directors until 2025 and served as Chairman of its board of directors until 2025. He has also founded or co-founded several other biopharmaceutical companies, including Genmab A/S, Veloxis A/S (f/k/a Life Cycle Pharma A/S), Zealand Pharma A/S and Acadia Pharmaceuticals Inc. Mr. Schönharting has more than 25 years of investment executive experience in public and private equity funds involved in the biopharmaceutical industry. We believe that Mr. Schönharting is qualified to serve on our Board of Directors because of his experience, attributes and skills, including his extensive pharmaceutical and executive experience.

***Michael Forer*,** has served as the Vice Chairman of our Board of Directors since March 2022 and as a member of our Board of Directors since December 2020. Mr. Forer was a co-founder of ADC Therapeutics SA in 2011 and has served as its initial Chief Executive Officer from 2011 to 2015, its Vice Chairman from 2015 to 2023, its Chief Financial Officer through its IPO on the NYSE from 2015 to 2020, its Executive Vice President from 2015 to 2022 and General Counsel from 2020 to 2022. Previously, Mr. Forer was a board member and Executive Director of Spirogen Sarl from 2008 to 2013, leading up to its acquisition by AstraZeneca in 2013 for $440 million. Mr. Forer has extensive experience as a professional investor in the biotech sector, including leading investments in Spirogen and ADC Therapeutics for Auven Therapeutics Holdings L.P. from 2008 to 2015, as a co-founder and partner in Rosetta Capital Limited from 2001 to present, and as an investment manager at Rothschild Asset Management from 1998 to 2001. Mr. Forer holds a B.A. in Economics from the University of Western Ontario and an LL.B. from the University of British Columbia. We believe that Mr. Forer is qualified to serve on our Board of Directors because of his experience, attributes and skills, including his extensive pharmaceutical experience.

Dermot Hanley, has served as a member of our Board of Directors since September 2021. Mr. Hanley is an experienced independent non-executive director and investment banker. He is currently a non-executive board member of numerous private equity backed companies and regulated financial investment funds. These include several group companies of Killiney Maritime II since September 2018 and January 2023, respectively, Larix Opportunities Master ICAV since February 2020 and Varagon Capital Credit Strategies ICAV since October 2020. Additionally, he serves as Chairperson of RTW Royalty ICAV (previously RTW Investment ICAV) since January 2021, 4010 Royalty Investments ICAV and 4010 Investments Fund GP LLC since May 2023, BFO Apogem GP Limited since May 2024, Arcano Direct Lending ICAV I since November 2025, Arcano Direct Lending ICAV II since February 2026, and Chesapeake ICAV IV since February 2026. He founded Nusli in 2012. Previously, Mr. Hanley was Co-Head of Coverage for Barclays Bank Ireland and spent 16 years in international investment banking and capital markets roles with major global firms, including Claret Capital, JP Morgan, Deutsche Bank and Citibank. He is a member of the Governance Advisory Council for The Corporate Governance Institute and was previously a longstanding member of the Finance and Economics Committee (Ecotax) at The Irish Business and Employers Confederation. He is a graduate of University College Dublin (BSc) and The Queen's University of Belfast (MBA) and holds a diploma in corporate governance from The Corporate Governance Institute/Glasgow Caledonia University. We believe that Mr. Hanley is qualified to serve on our Board of Directors because of his experience, attributes and skills, including his extensive executive experience.

Duncan Moore, PhD, has served as a member of our Board of Directors since September 2021. Dr. Moore is a partner at East West Capital Partners since May 2008. Previously, Dr. Moore was a top-ranked pharmaceutical analyst at Morgan Stanley from 1991 to 2008 and was a Managing Director from 1997 to 2008 leading the firm's global healthcare equity research team. Whilst at the University of Cambridge, he co-founded a medical diagnostics company, Ultra Clone, with two colleagues which led to the beginnings of a 20-year career in healthcare capital markets analysis. In 1986, he was involved in establishing the BankInvest biotechnology funds and was on their scientific advisory board. Dr. Moore was educated in Edinburgh and attended the University of Leeds where he studied Biochemistry and Microbiology. He has a M.Phil. and Ph.D. from the University of Cambridge where he was also a post-doctoral research fellow. He served on the board of directors of Forward Pharma A/S until 2025. Currently, he is an active investor in biomedical companies and he has a board position at Cycle Pharma and ASP Isotopes. He is also the Chairman of the Scottish Life Sciences Association and serves on the Board of Governors of Merchiston Castle School in Edinburgh and the International School in Shenzhen in the Peoples Republic of China. We believe that Dr. Moore is qualified to serve on our Board of Directors because of his experience, attributes and skills, including his extensive pharmaceutical and executive experience.

B. Compensation

Compensation of Directors and Executive Officers

For the year ended December 31, 2025, the aggregate compensation paid to the members of our Board of Directors and our executive officers for services in all capacities, including retirement and similar benefits, was $9.2 million.

During the year ended December 31, 2025, GH Research PLC granted options to purchase an aggregate of 494,001 ordinary shares to members of our Board of Directors and executive officers. 480,000 of these share options were granted to our executive officers which vest 25% on the first anniversary of the date of grant, and thereafter in equal installments on a monthly basis over the subsequent three years. The contractual term (expiration) of these share options is seven years from the grant date with a weighted-average exercise price of $0.025. 14,001 of these share options were granted to members of our Board of Directors which were fully vested on the date of grant and are subject to a two-year service condition. The contractual term (expiration) of these share options is seven years from the grant date with a weighted-average exercise price of $0.025.

Equity Incentive Plans

Share Option Plan

We have adopted a share option plan (referred to herein as the Share Option Plan), under which grants of options are made to eligible participants. The purpose of the Share Option Plan is to attract, retain and motivate employees and directors to provide for competitive compensation opportunities, to encourage long term service, to recognize individual contributions and reward achievement of performance goals, and to promote the creation of long term value for our shareholders. In 2025, our Board of Directors approved an amendment to our Share Option Plan to increase the amount of ordinary shares that may be issued pursuant to future option grants under such plan by 1,518,547 shares. As of December 31, 2025, options with respect to 2,594,914 ordinary shares, having a weighted average exercise price of $3.87 per share, were outstanding under the Share Option Plan.

Plan Administration: The Share Option Plan is administered by our remuneration committee and is subject to the remuneration committee's discretion to delegate such authority to other members of our board or our officers or managers.

Eligible Participants: Under the Share Option Plan, any director (including our directors and directors of any other member of our group who are not active employees of the Company or any other company that is a member of our group) or employee of a member of the group or key consultant (referred to herein as the Eligible Person) is eligible to be nominated by our remuneration committee to receive options. The remuneration committee retains absolute discretion in determining whether or not the Eligible Person shall be nominated to participate in the Share Option Plan. No person is entitled as of right to participate in the Share Option Plan.

Awards: The number of ordinary shares in respect of which options may be granted under the Share Option Plan will not, when added to the number of ordinary shares which have been or remain to be issued or purchased pursuant to options granted during the immediately preceding 10-year period, exceed 3,721,251 ordinary shares, until otherwise resolved by the remuneration committee. Under the Share Option Plan, equity will be awarded in the form of options. Options will have an exercise price determined by the remuneration committee but will not (unless otherwise determined) be less than the market value of an ordinary share on the day preceding the date of grant. The term of each option will be determined by the remuneration committee, but will not be longer than eight years from the date of grant.

Limitation as to Participation: Under the Share Option Plan, no option will be capable of being granted more than 10 years from the date of adoption of the Share Option Plan.

Participation: The conditions for participation in the Share Option Plan, including the time or times at which options may be exercised, will be determined by the remuneration committee and set forth in the applicable option plan documentation. Unless otherwise outlined, the options will be personal to the participant and will lapse if a participant purports to assign, transfer, sell, mortgage, pledge or encumber the option.

Termination of Service and Change in Control: In the event of a participant's termination of employment or service, (1) any part of an option that has not vested as of the date of cessation will lapse immediately, and (2) any part of an option that has vested as at the date of cessation will lapse in full 30 days after the date of cessation to the extent not exercised by such date.

If a participant dies, the remuneration committee may determine that either the whole or a specified percentage of any option held by such participant at the date of their death will be capable of vesting, or being exercised by or otherwise transferred to their legal personal representative.

In the event of a participant's termination of employment where such participant is considered a good leaver, the remuneration committee may in its absolute discretion determine the extent to which the option may be vested or exercised.

In the event that the Company or the subsidiary is party to a merger, a sale of all or substantially all of its assets, a takeover or other reorganization, the remuneration committee will be entitled to, in its discretion, (1) accelerate the vesting of the whole or a specified portion of the options, (2) agree that outstanding options will be assumed or substituted by the surviving company or its parent for options which are equivalent to the options originally granted under the plan but which relate to shares in the surviving company or its parent, (3) arrange for the continuation of outstanding options, (4) make payment of a cash settlement to the participants equal (per share) to the amount to be paid for one share under the agreement of merger or takeover, or (5) vary the outstanding options on such terms as the committee may decide.

Termination and Amendment: Unless terminated earlier by resolution of the Company or the Board of Directors, the Share Option Plan will continue for a term of 10 years. Our remuneration committee may at any time by resolution amend or revoke any provision of the Share Option Plan subject to shareholder approval if required by applicable law or stock exchange rules. However, no such action may materially adversely affect the rights of the participant of any options unless agreed to by the participant.

Employment Agreements

We have entered into employment agreements with our executive officers. Each of these agreements provides for an initial salary, and generally requires advance notice of termination, typically six months. Our executive officers have agreed to covenants not to compete against us or solicit our employees or customers during employment and for a period of up to 12 months following termination.

C. Board Practices

Board Composition of Directors

Our Board of Directors is composed of four members. The current members of our Board of Directors were reelected at our annual general meeting of shareholders in 2025 and will serve until our next annual general meeting in 2026.

Our Board of Directors has determined that each of Michael Forer, Dermot Hanley and Duncan Moore qualifies as an independent director within the meaning of applicable Nasdaq standards.

There is no service contract between any of our directors and either us or our subsidiary, which provides for any benefits upon termination of employment.

We are a foreign private issuer under the rules of the SEC. As a result, in accordance with Nasdaq listing requirements, we will continue to rely on home country governance requirements and certain exemptions thereunder rather than on the stock exchange corporate governance requirements. There are no family relationships among any of our directors or executive officers. For an overview of our corporate governance principles, see “Item 10. Additional Information—B. Memorandum and Articles of Association” and “Item 16G—Corporate Governance.”

Committees of the Board of Directors

Our Board of Directors has established a separate audit committee, nominating and corporate governance committee and remuneration committee.

Audit Committee

The audit committee, which consists of Dermot Hanley (Chair), Michael Forer and Duncan Moore, assists our Board of Directors in overseeing our accounting and financial reporting processes and the audits of our financial statements. In addition, the audit committee is directly responsible for the compensation, retention and oversight of the work of our independent registered public accounting firm that our shareholders elect as our external auditors. The audit committee consists exclusively of members of our Board of Directors who are financially literate, and each of Dermot Hanley, Michael Forer and Duncan Moore is considered an “audit committee financial expert” as defined by the SEC. Our Board of Directors has determined that each of Dermot Hanley, Michael Forer and Duncan Moore satisfies the “independence” requirements set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended.

The audit committee is governed by a charter that complies with Nasdaq rules that apply to us. The audit committee has the responsibility for, among other things:

- recommending the appointment of the independent auditor to shareholders for approval at the general meeting of shareholders;
- the appointment, compensation, retention and oversight of any accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit services;
- pre-approving the audit services and non-audit services to be provided by our independent auditor before the auditor is engaged to render such services;
- evaluating the independent auditor's qualifications, performance and independence, and presenting its conclusions to the full Board of Directors on at least an annual basis;
- reviewing and discussing with management and our independent registered public accounting firm our financial statements and our financial reporting process; and
- reviewing, approving or ratifying any related party transactions.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee, which consists of Florian Schönharting (Chair) and Michael Forer, assists our Board of Directors in identifying individuals qualified to become members of the Board of Directors and recommends to the Board of Directors the director nominees for the next annual general meeting of shareholders or to fill an existing or newly created vacancy on the Board of Directors.

The nominating and corporate governance committee has the responsibility for, among other things:

- drawing up selection criteria and appointment procedures for directors;
- assessing the functioning of individual members of our Board of Directors and executive officers and reporting the results of such assessment to our Board of Directors;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by shareholders;
- reviewing the composition of our Board of Directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- recommending to our Board of Directors the persons to be nominated for election as directors and to each of our Board of Directors' committees;
- developing and recommending to our Board of Directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our Board of Directors and management.

Remuneration Committee

The remuneration committee, which consists of Michael Forer (Chair) and Florian Schönharting, assists our Board of Directors in setting the remuneration of the Board of Directors, executive officers of the Company and such other members of senior management as the committee is designated by the Board of Directors to set remuneration for.

The remuneration committee has the responsibility for, among other things:

- identifying, reviewing and proposing policies relevant to the compensation and benefits of our directors and executive officers;
- evaluating the performance of senior management in light of such policies and reporting to the board; and
- overseeing and administering our employee share option scheme or equity incentive plans in operation from time to time.

D. Employees

As of December 31, 2025, we employed seventy-three people. Fifty-six employees are engaged in research and development activities with the rest providing administrative, business and operations support. None of our employees are represented by labor unions or covered by collective bargaining agreements. We have not experienced any employee litigation or claims and consider our employee relations to be good.

E. Share Ownership

See "Item 7. Major Shareholders and Related Party Transactions—A. Major Shareholders."

F. Disclosure of a Registrant's Action to Recover Erroneously Awarded Compensation

Not applicable.

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders

The following table presents information relating to the beneficial ownership of our ordinary shares as of December 31, 2025:

- each person, or group of affiliated persons, known by us to own beneficially 5% or more of our outstanding ordinary shares;
- each of our executive officers and directors; and
- all executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. Under those rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. Except as otherwise indicated, and subject to community property laws where applicable, we believe, based on the information provided to us, that the persons and entities named in the table below have sole voting and investment power with respect to all ordinary shares shown as beneficially owned by them.

The percentage of beneficial ownership in the table below is based on 62,029,395 ordinary shares outstanding as of February 17, 2026. Options to purchase shares that are exercisable within 60 days are deemed to be beneficially owned by the persons holding these options for the purpose of computing percentage ownership of that person, but are not treated as outstanding for the purpose of computing any other person's ownership percentage.

As of February 17, 2026, to our knowledge, 4 U.S. record holders held approximately 83.6% of our issued and outstanding ordinary shares. The actual number of shareholders is greater than this number of record holders and includes shareholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include shareholders whose shares may be held in trust or by other entities.

Except as otherwise indicated in the table below, addresses of the directors, executive officers and named beneficial owners are in care of GH Research PLC, Joshua Dawson House, Dawson Street, Dublin 2, D02 RY95, Ireland.

Principal Shareholders	Number of Ordinary Shares Beneficially Owned	Percentage of Ordinary Shares Beneficially Owned
5% or Greater Shareholders		
Lynx1 Capital Management LP(1)	10,406,575	16.8%
BVF(2)	8,827,712	14.2%
RA Capital(3)	7,676,697	12.4%
RTW Investments LP(4)	5,933,815	9.6%
FMR LLC(5)	5,136,045	8.3%
Executive Officers and Directors		
Velichka Valcheva	*	*
Magnus Halle	*	*
Julie Ryan	*	*
Aaron Cameron	*	*
Florian Schönharting	14,824,419	23.9%
Michael Forer	*	*
Dermot Hanley	*	*
Duncan Moore	*	*
All executive officers and directors as a group (8 persons)	15,505,629	24.8%

* Represents beneficial ownership of less than 1% of our total outstanding ordinary shares.

(1) Based solely on the 13G/A filed with the SEC by Lynx1 Capital Management LP (the "Investment Manager") on February 17, 2026 and consists of ordinary shares held by Lynx1 Master Fund LP (the "Lynx1 Fund") and a managed account. Mr. Weston Nichols, the sole member of Lynx1 Capital Management GP LLC, the general partner of the Investment Manager, may be deemed a beneficial owner for purposes of Section 13(d) of the Exchange Act with respect to the Ordinary Shares directly held by the Lynx1 Fund and the managed account. The address of the Investment Manager is D81 Calle C Suite 301, PMB 1202 Dorado, PR, 00646-2051 and the address of Weston Nichols is c/o Lynx1 Capital Management LP, D81 Calle C Suite 301, PMB 1202 Dorado, PR, 00646-2051.

(2) Based solely on the Form 13F Holdings Report filed with the SEC by BVF Inc. on February 17, 2026 and consists of ordinary shares held by Biotechnology Value Fund, L.P. ("BVF"), including ordinary shares held by Biotechnology Value Fund II, L.P. ("BVF2") and Biotechnology Value Trading Fund OS L.P. ("Trading Fund OS"). BVF ("BVF GP"), as the general partner of BVF, may be deemed to beneficially own the shares beneficially owned by BVF. BVF II GP L.L.C. ("BVF2 GP"), as the general partner of BVF2, may be deemed to beneficially own the shares beneficially owned by BVF2. BVF Partners OS Ltd. ("Partners OS"), as the general partner of Trading Fund OS, may be deemed to beneficially own the shares beneficially owned by Trading Fund OS. BVF GP Holdings L.L.C. ("BVF GPH"), as the sole member of each of BVF GP and BVF2 GP, may be deemed to beneficially own the shares beneficially owned in the aggregate by BVF and BVF2. BVF Partners L.P. ("Partners"), as the general partner of BVF and BVF2, the sole member of Partners OS, and the investment manager of Trading Fund OS, may be deemed to beneficially own the shares beneficially owned in the aggregate by BVF, BVF2 and Trading Fund OS. BVF Inc., as the general partner of Partners, may be deemed to beneficially own the shares beneficially owned by Partners. Mark Lampert, as a director and officer of BVF Inc., may be deemed to beneficially own the shares beneficially owned by BVF Inc. The address of the above persons and entities is 44 Montgomery Street, 40th Floor, San Francisco, CA 94104.

(3) Based solely on the Form 13F Holdings Report filed with the SEC by RA Capital Management, L.P. ("RA Capital") on February 17, 2026 and consists of ordinary shares held by RA Capital Healthcare Fund, L.P. (the "Fund") and RA Capital Nexus Fund II, L.P. (the "Nexus Fund II"). RA Capital Healthcare Fund GP, LLC is the general partner of the Fund and RA Capital Nexus Fund II GP, LLC is the general partner of the Nexus Fund II. The general partner of RA Capital is RA Capital Management GP, LLC, of which Dr. Kolchinsky and Mr. Shah are the controlling persons. RA Capital serves as investment advisor for the Fund and the Nexus Fund II and may be deemed a beneficial owner, for purposes of Section 13(d) of the Exchange Act, of any securities held by the Fund and the Nexus Fund II. The Fund and the Nexus Fund II have delegated to RA Capital the sole power to vote and the sole power to dispose of all securities held in the Fund's and the Nexus Fund II's portfolios, including the Company's ordinary shares. As managers of RA Capital, Dr. Kolchinsky and Mr. Shah may be deemed beneficial owners, for purposes of Section 13(d) of the Exchange Act, of any securities beneficially owned by RA Capital. The address of RA Capital is 200 Berkeley Street, 18th Floor, Boston MA 02116.

(4) Based solely on the Form 13F Holdings Report filed with the SEC by RTW Investments, LP on February 17, 2026 and consists of ordinary shares directly held by certain funds (the "RTW Funds") to which RTW Investments serves as investment advisor. As a result, RTW Investments may be deemed a beneficial owner of the ordinary shares directly held by the RTW Funds. Dr. Roderick Wong serves as Managing Partner and Chief Investment Officer of RTW Investments, and as a result may also be deemed a beneficial owner of any securities directly held by the RTW Funds. The address of the business office of the above persons and entities is 40 10th Avenue, Floor 7, New York, New York 10014.

(5) Based solely on the Form 13F Holdings Report filed with the SEC by FMR LLC on February 17, 2026 and consists of ordinary shares directly held by FMR LLC or certain of its subsidiaries and affiliates.Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. The address of FMR LLC is 245 Summer Street, Boston, Massachusetts 02210.

B. Related Party Transactions

The following is a description of related party transactions we have entered into since January 1, 2025, with any members of our Board of Directors, our executive officers and the holders of more than 5% of our ordinary shares, other than compensation arrangements which are described under "Item 6. Directors, Senior Management and Employees."

Indemnification

Our Constitution requires us to indemnify our directors and executive officers, employees and other officials serving at the specific direction of the Company to the fullest extent permitted by Irish law. For more information, see Exhibit 2.1 to this Annual Report.

Related Person Transaction Policy

We have adopted a related person transaction policy, which states that any related person transaction must be approved or ratified by our Board of Directors or a designated committee thereof. In determining whether to approve or ratify a transaction with a related person, our Board of Directors or the designated committee will consider all relevant facts and circumstances, including without limitation the commercial reasonableness of the terms, the benefit and perceived benefit, or lack thereof, to us, opportunity costs of alternate transactions, the materiality and character of the related person's direct or indirect interest and the actual or apparent conflict of interest of the related person. Our Board of Directors or the designated committee will not approve or ratify a related person transaction unless it has determined that, upon consideration of all relevant information, such transaction is in, or not inconsistent with, our best interests and the best interests of our shareholders.

C. Interests of Experts and Counsel

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. Consolidated Statements and Other Financial Information

Financial Statements

See "Item 18. Financial Statements," which contains our financial statements prepared in accordance with IFRS Accounting Standards.

Legal Proceedings

From time to time, we may be a party to litigation or subject to claims incident to the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, we currently believe that the final outcome of these ordinary course matters will not have a material adverse effect on our results of operations, cash flows and financial position. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors. We were not a party to any material litigation and did not have material contingency reserves established for any liabilities as of December 31, 2025.

Dividends and Dividend Policy

We have never declared or paid cash dividends on our share capital. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our Board of Directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our Board of Directors may deem relevant.

Under Irish law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized, less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital. In addition, no distribution or dividend may be made if our net assets are not, or if making such distribution or dividend will cause our net assets to not be, equal to or in excess of the aggregate of our called up share capital plus undistributable reserves.

As we are an Irish company, Irish dividend withholding tax, or DWT, currently at a rate of 25%, will arise in respect of dividends or other distributions to our shareholders unless an exemption applies. There are exemptions that may be available to U.S. Holders (as defined in "Item 10. Additional Information—E. Taxation"); such shareholders should consult their respective tax advisors. Where DWT arises, we are responsible for deducting DWT at source and accounting for the relevant amount to the Revenue Commissioners of Ireland. See "Item 10. Additional Information—B. Memorandum and Articles of Association."

B. Significant Changes

A discussion of the significant changes in our business can be found under "Item 4. Information on the Company—A. History and Development of the Company" and "Item 4. Information on the Company—B. Business Overview."

ITEM 9. THE OFFER AND LISTING

A. Offer and Listing Details

See "—C. Markets" below.

B. Plan of Distribution

Not applicable.

C. Markets

Our ordinary shares are listed on Nasdaq under the symbol "GHRS." For a description of our ordinary shares, see "Item 10. Additional Information—B. Memorandum and Articles of Association."

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the Issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share Capital

Not applicable.

B. Memorandum and Articles of Association

Exhibit 2.1 to this Annual Report, which contains a description of our ordinary shares and our Constitution, is incorporated herein.

C. Material Contracts

Except as otherwise disclosed in this Annual Report (including the Exhibits), we are not currently, and have not been in the last two years, party to any material contract, other than contracts entered into in the ordinary course of business.

D. Exchange Controls

Under the laws of Ireland, except as indicated below, there are currently no restrictions on the export or import of capital, including foreign exchange controls or restrictions that affect the remittance of dividends, interest or other payments to non-resident holders of our ordinary shares.

The Financial Transfers Act, 1992 gives power to the Minister for Finance of Ireland to make provision for the restriction of financial transfer between Ireland and other countries and persons. Financial transfers are broadly defined, and include all transfers which would be movements of capital or payments within the meaning of the treaties governing the European Communities. The acquisition or disposal of shares issued by an Irish incorporated company and associated payments may fall within this definition. In addition, dividends or payments on redemption or purchase of shares and payments on a liquidation of an Irish incorporated company would fall within this definition.

To date, the Minister of Finance of Ireland has restricted financial transfers between Ireland and a number of third countries and persons, and the list is subject to on-going change.

The Screening of Third Country Transactions Act 2023 of Ireland, or the FDI Act, has established a foreign direct investment screening system in Ireland. The FDI Act requires parties to certain acquisition and/or investment transactions involving (i) Irish companies and business undertakings in a range of sectors (including critical health infrastructure); and (ii) acquiring/investing parties established in countries outside of the EEA and Switzerland, or third countries, to provide notice of such transactions to the Irish Minister for Enterprise, Trade and Employment for prior approval. The Minister would then determine if the relevant transaction poses a risk to Ireland's security or public order and may, where deemed appropriate, prevent the transaction from being consummated or otherwise impose conditions on the transaction. The Minister may also review transactions for which he/she has not received notice, if the Minister has reasonable grounds for believing that a given transaction poses a risk to Ireland's security or public order, whether such transaction has been completed or not. The FDI Act involves increased information sharing and co-operation with other Member States of the EU in light of the EU Investment Screening Regulation (Regulation (EU) 2019/452).

E. Taxation

The following discussion is based on the tax laws, regulations and regulatory practices of the United States and Ireland as in effect on the date hereof, which are subject to change (or subject to changes in interpretation), possibly with retroactive effect.

Current and prospective shareholders are advised to consult their own tax advisors in light of their particular circumstances as to the U.S. or Irish tax laws, regulations and regulatory practices that could be relevant for them in connection with owning and selling or otherwise disposing of our ordinary shares and receiving dividends and similar cash or in-kind distributions on our ordinary shares (including dividends on liquidation proceeds and share dividends) or distributions on our ordinary shares based upon a capital reduction or reserves paid out of capital contributions and the consequences thereof under the tax laws, regulations and regulatory practices of the United States or Ireland.

Material U.S. Federal Income Tax Consequences for U.S. Holders

The following is a description of the material U.S. federal income tax consequences to U.S. Holders, as defined below, of owning and disposing our ordinary shares. It does not describe all tax consequences that may be relevant to a particular person's decision to acquire ordinary shares.

This discussion applies only to a U.S. Holder that holds ordinary shares as capital assets for U.S. federal income tax purposes (generally, property held for investment). In addition, it does not describe any tax consequences other than U.S. federal income tax consequences, including state and local tax consequences and estate tax consequences, and does not describe all of the U.S. federal income tax consequences that may be relevant in light of the U.S. Holder's particular circumstances, including alternative minimum tax consequences, the potential application of the provisions of the Code known as the Medicare contribution tax, special tax accounting rules under Section 451(b) of the Code, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- certain banks, insurance companies and other financial institutions;
- brokers, dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding ordinary shares as part of a straddle, wash sale, conversion transaction or other integrated transaction or persons entering into a constructive sale with respect to the ordinary shares;
- persons whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;
- entities or arrangements classified as partnerships or S corporations for U.S. federal income tax purposes (and investors therein);
- tax-exempt entities, including an "individual retirement account" or "Roth IRA," or governmental entities;
- real estate investment trusts or regulated investment companies;
- former U.S. citizens or long-term residents of the United States;
- persons that own or are deemed to own 10% or more of the voting power or value of our shares;
- persons who acquired our ordinary shares pursuant to the exercise of an employee stock option or otherwise as compensation; or

- persons holding ordinary shares in connection with a trade or business conducted outside of the United States or in connection with a permanent establishment or other fixed place of business outside of the United States.

If an entity or arrangement that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding ordinary shares and partners in such partnerships should consult their tax advisors as to the particular U.S. federal income tax consequences of owning and disposing of the ordinary shares in their circumstances.

This discussion is based on the Code, administrative pronouncements, judicial decisions, final, temporary and proposed U.S. Treasury regulations, and the income tax treaty between Ireland and the United States, or the Treaty, all as of the date hereof, any of which is subject to change or differing interpretations, possibly with retroactive effect.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares, who is eligible for the benefits of the Treaty and who is:

- a citizen or individual resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia; or
- an estate or trust the income of which is subject to U.S. federal income taxation regardless of its source.

U.S. Treasury regulations that apply to taxable years beginning on or after December 28, 2021, or the Foreign Tax Credit Regulations, may in some circumstances prohibit a U.S. person from claiming a foreign tax credit with respect to certain non-U.S. taxes that are not creditable under applicable income tax treaties. The U.S. Internal Revenue Service, or the IRS, has released notices which indicate that the U.S. Treasury Department and the IRS are considering amendments to the Foreign Tax Credit Regulations and provide temporary relief from certain of their provisions until such time as the IRS issues a subsequent notice or other guidance withdrawing or modifying the temporary relief (or any later date specified in the relevant notice or guidance). U.S. investors that are not eligible for Treaty benefits should consult their tax advisors regarding the creditability or deductibility of any non-U.S. taxes imposed on them. This discussion does not apply to investors in this special situation. U.S. Holders should consult their tax advisors concerning the U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of ordinary shares in their particular circumstances.

Passive Foreign Investment Company Rules

Under the Code, we will be a PFIC for any taxable year in which, after the application of certain "look-through" rules with respect to our subsidiaries, either (i) 75% or more of our gross income consists of "passive income," or (ii) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, "passive income." For purposes of the calculations above, we will be treated as if we hold our proportionate share of the assets of, and receive directly our proportionate share of the income of, any other corporation in which we directly or indirectly own at least 25%, by value, of the shares of such corporation. Passive income generally includes dividends, interest, rents, certain non-active royalties, and capital gains. Based on our current operations, income, assets and certain estimates and projections, including as to the relative values of our assets, including goodwill, which is based on the price of our ordinary shares, we believe that we were a PFIC for our 2025 taxable year due to the interest income we recognized (which is passive income for purposes of the PFIC rules) and the fact that we generated no other active income. Additionally, we expect a similar income composition in 2026 and, therefore, we anticipate that we will likely be a PFIC in 2026 and may also be a PFIC in future taxable years. However, because our PFIC status is a factual annual determination that can be made only after the end of the relevant taxable year, our PFIC status for 2026 or any future taxable year is uncertain. If we are a PFIC for any year during which a U.S. Holder holds ordinary shares, we would generally continue to be treated as a PFIC with respect to such holder for all succeeding years during which such holder holds ordinary shares, even if we ceased to meet the threshold requirements for PFIC status, unless the U.S. Holder makes a "deemed sale" election, which would allow the U.S. Holder to eliminate the continuing PFIC status under certain circumstances but would require the U.S. Holder to recognize gain taxed under the general PFIC rules described below. Prospective investors should invest in our ordinary shares only if they are willing to bear the U.S. federal income tax consequences associated with an investment in a PFIC.

If we were a PFIC for any taxable year and any of our subsidiaries or other companies in which we owned or were treated as owning equity interests were also a PFIC (any such entity is herein referred to as a "Lower-tier PFIC"), a U.S. Holder would be deemed to own a proportionate amount (by value) of the shares of each Lower-tier PFIC and would be subject to U.S. federal income tax according to the rules described in the subsequent paragraph on (i) certain distributions by a Lower-tier PFIC; and (ii) dispositions of shares of Lower-tier PFICs, in each case as if such holder held such shares directly, even though such holder will not have received the proceeds of those distributions or dispositions.

If we were a PFIC for any taxable year during which a U.S. Holder held any of our ordinary shares, such holder would generally be subject to adverse tax consequences. Generally, gain recognized upon a disposition (including, under certain circumstances, a pledge) of our ordinary shares would be allocated ratably over a U.S. Holder's holding period for the ordinary shares. The amounts allocated to the taxable year of disposition and to years before we became a PFIC would be taxed as ordinary income. The amount allocated to each other taxable year would be subject to tax at the highest rate in effect for that taxable year for individuals or corporations, as appropriate, and an interest charge would be imposed on the tax on such amount. Further, to the extent that any distributions received on a U.S. Holder's ordinary shares during a taxable year exceeded 125% of the average of the annual distributions on those shares during the preceding three years or such holder's holding period, whichever was shorter, those distributions would be subject to taxation in the same manner as gain.

Alternatively, if we were a PFIC and if the ordinary shares were "regularly traded" on a "qualified exchange," a U.S. Holder may avoid the general PFIC tax consequences discussed above if such U.S. Holder makes a mark-to-market election with respect to the ordinary shares at the close of the first taxable year in which such holder holds our ordinary shares. Nasdaq, on which the ordinary shares are listed, is a qualified exchange for this purpose. Once made, the election cannot be revoked without the consent of the IRS unless the ordinary shares cease to be marketable.

If a U.S. Holder makes the mark-to-market election with respect to the first taxable year that we are a PFIC and the U.S. Holder holds our ordinary shares, such holder will generally recognize as ordinary income any excess of the fair market value of such holder's ordinary shares at the end of each taxable year in which we are a PFIC over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the ordinary shares over their fair market value at the end of such taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). The U.S. Holder's tax basis in their ordinary shares will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of ordinary shares in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). Any gain or loss recognized on the sale or other disposition of ordinary shares in a year when we are not a PFIC will generally be taxed in the manner described below under "—Sale or Other Disposition of Ordinary Shares." Subject to the discussion in the immediately succeeding paragraph, any distributions will generally be taxed in a manner described below under "—Taxation of Distributions." This election will not apply to any of our non-U.S. subsidiaries. Accordingly, a U.S. Holder may continue to be subject to tax under the PFIC excess distribution regime with respect to any Lower-tier PFICs notwithstanding a mark-to-market election for the ordinary shares.

In addition, if we were a PFIC for any taxable year in which we paid a dividend or for the prior taxable year, the preferential dividend rates discussed below with respect to dividends paid to certain non-corporate U.S. Holders would not apply.

If a company that is a PFIC provides certain information to U.S. Holders, a U.S. Holder can then avoid certain adverse tax consequences described above by making a "qualified electing fund" ("QEF Election") in the first taxable year that the company is treated as a PFIC with respect to the U.S. Holder. A U.S. Holder must make the QEF Election for each PFIC by attaching a separate properly completed IRS Form 8621 for each PFIC to the U.S. Holder's timely filed U.S. federal income tax return.

We will endeavor to provide information necessary for U.S. Holders to make a QEF Election with respect to us for the 2025 taxable year and currently intend to provide such information for any subsequent year if we believe we are a PFIC in such year, but there is no assurance that we will timely provide this information. Moreover, even if we provide this information regarding us and any wholly-owned subsidiaries on a timely basis, we may not be able to furnish this information with respect to a non-wholly-owned Lower-tier PFIC, if any. There is also no assurance that we will have timely knowledge of our status as a PFIC in the future or of the information that a U.S. Holder would need to provide in order to make a valid election.

If a U.S. Holder makes a QEF Election with respect to a PFIC, the U.S. Holder will be taxed on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is a PFIC. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the U.S. Holder's income under the QEF Election would not be taxable to the U.S. Holder. A U.S. Holder will increase its tax basis in its ordinary shares by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the ordinary shares that is not included in the U.S. Holder's income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of ordinary shares in an amount equal to the difference between the amount realized and the U.S. Holder's adjusted tax basis in the ordinary shares, as determined in U.S. dollars. U.S. Holders should note that if they make QEF Elections with respect to us or any Lower-tier PFICs, they may be required to pay U.S. federal income tax with respect to their ordinary shares for any taxable year significantly in excess of any cash distributions received on the ordinary shares for such taxable year. U.S. Holders should consult their tax advisors regarding making QEF Elections in their particular circumstances.

U.S. Holders should consult their tax advisors regarding whether we are a PFIC and the potential application of the PFIC rules.

If a U.S. Holder owns ordinary shares during any year in which we are a PFIC, the U.S. Holder generally must file an annual report on IRS Form 8621 with respect to us and any Lower-Tier PFICs containing such information as the U.S. Treasury may require, generally with the U.S. Holder's U.S. federal income tax return for the relevant year. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with respect to the items required to be included in such report until three years after the U.S. Holder files the annual report and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period.

PROSPECTIVE U.S. HOLDERS SHOULD CONSULT THEIR TAX ADVISORS REGARDING THE CONSEQUENCES OF OUR PFIC STATUS ON AN INVESTMENT IN ORDINARY SHARES.

Taxation of Distributions

The following is subject to the discussion under "—Passive Foreign Investment Company Rules" above. As discussed above under "Item 8. Financial Information—A. Consolidated Statements and Other Financial Information—Dividends and Dividend Policy," we do not currently expect to make distributions on our ordinary shares. In the event that we do make distributions of cash or other property, distributions paid on ordinary shares, other than certain pro rata distributions of ordinary shares, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we do not maintain calculations of our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. However, in light of the discussion in "—Passive Foreign Investment Company" above, non-corporate U.S. Holders should expect that dividends, if any, will likely not be eligible for preferential tax rates.

The amount of a dividend will include any amounts withheld by us in respect of Irish income taxes. The amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in Euros will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars at that time. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt.

Subject to applicable limitations, some of which vary depending upon the U.S. Holder's particular circumstances, Irish income taxes withheld from dividends on ordinary shares (at a rate not exceeding the rate provided by the Treaty) will be creditable against the U.S. Holder's U.S. federal income tax liability. The rules governing foreign tax credits are complex and U.S. Holders should consult their tax advisors regarding the creditability of foreign taxes in their particular circumstances. In lieu of claiming a foreign tax credit, U.S. Holders may, at their election, deduct foreign taxes, including any Irish income tax, in computing their taxable income, subject to generally applicable limitations under U.S. law. An election to deduct foreign taxes instead of claiming foreign tax credits applies to all foreign taxes paid or accrued in the taxable year.

Sale or Other Disposition of Ordinary Shares

The following is subject to the discussion under "—Passive Foreign Investment Company Rules" above.

Gain or loss realized by a U.S. Holder on the sale or other disposition of ordinary shares will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder's holding period for such ordinary shares was more than one year as of the date of the sale or other disposition. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the ordinary shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. Long-term capital gain recognized by a non-corporate U.S. Holder is subject to U.S. federal income tax at rates lower than the rates applicable to ordinary income and short-term capital gains, while short-term capital gains are subject to U.S. federal income tax at the rates applicable to ordinary income. However, in light of the discussion under "—Passive Foreign Investment Company" above, U.S. Holders should expect that any gain recognized on a sale or other taxable disposition of the ordinary shares will likely not be treated as long-term capital gain. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to various limitations.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and certain entities) may be required to report information relating to an interest in our ordinary shares, subject to certain exceptions (including an exception for ordinary shares held in accounts maintained by certain U.S. financial institutions). U.S. Holders should consult their tax advisors regarding the effect, if any, of this legislation on their ownership and disposition of the ordinary shares.

Material Irish Tax Consequences

The following is a summary of the material Irish tax consequences for certain beneficial holders of ordinary shares. The summary is based upon Irish tax laws and the practice of the Revenue Commissioners of Ireland in effect on the date of this Annual Report and correspondence with the Revenue Commissioners of Ireland. Changes in law and/or administrative practice may result in alteration of the tax considerations described below, possibly with retrospective effect.

The summary does not constitute tax advice and is intended only as a general guide. The summary is not exhaustive and holders of ordinary shares should consult their own tax advisors about the Irish tax consequences (and the tax consequences under the laws of other relevant jurisdictions) related to the acquisition, ownership and disposal of ordinary shares. The summary applies only to shareholders who will own ordinary shares as capital assets and does not apply to other categories of shareholders, such as dealers in securities, trustees, insurance companies, collective investment schemes and shareholders who have, or who are deemed to have, acquired ordinary shares by virtue of an Irish office or employment (performed or carried on in Ireland) or who are associated entities with respect to GH Research PLC (within the meaning of section 817U of the Taxes Consolidation Act, 1997).

Tax on Chargeable Gains

The current rate of tax on chargeable gains (where applicable) in Ireland is 33%.

A disposal of our ordinary shares by a shareholder who is not resident or ordinarily resident for tax purposes in Ireland will not give rise to Irish tax on any chargeable gain realized on such disposal unless such ordinary shares are used, held, or acquired for the purposes of a trade or business carried on by such shareholder in Ireland through a branch or agency.

A holder of our ordinary shares who is an individual and who is temporarily non-resident in Ireland may, under Irish anti-avoidance legislation, be liable to Irish tax on any chargeable gain realized on a disposal of our ordinary shares during the period in which such individual is non-resident.

Stamp Duty

The rate of stamp duty (where applicable) on transfers of shares of Irish incorporated companies is typically 1% of the price paid or the market value of the shares acquired, whichever is greater. Where Irish stamp duty arises, it is generally a liability of the transferee.

***Shares Held Through the* Depository Trust Company**

A transfer of our ordinary shares effected by means of the transfer of book entry interests through the Depository Trust Company, which is referred to in this Annual Report as "DTC", will not be subject to Irish stamp duty.

Shares Held Outside of DTC or Transferred Into or Out of DTC

A transfer of our ordinary shares where any party to the transfer holds such shares outside of DTC may be subject to Irish stamp duty, subject to the availability of a relief or exemption. Shareholders wishing to transfer their shares into (or out of) DTC may do so without giving rise to Irish stamp duty provided that:

- there is no change in the beneficial ownership of such shares as a result of the transfer; and
- the transfer into (or out of) DTC is not effected in contemplation of a sale of such shares by a beneficial owner to a third party.

Withholding Tax on Dividends

We do not expect to pay dividends for the foreseeable future. To the extent that we do make dividend payments (or other returns to shareholders that are treated as "distributions" for Irish tax purposes), it should be noted that such distributions made by us will, in the absence of one of many exemptions, be subject to Irish dividend withholding tax, which is referred to in this Annual Report as DWT, currently at a rate of 25%.

For DWT purposes, a distribution includes any distribution that may be made by us to our shareholders, including cash dividends, non-cash dividends and additional stock taken in lieu of a cash dividend. Where an exemption does not apply in respect of a distribution made to a particular shareholder, we are responsible for withholding DWT prior to making such distribution.

General Exemptions

The following is a general overview of the scenarios where it will be possible for us to make payments of dividends without deduction of DWT.

Irish domestic law provides that a non-Irish resident shareholder is not subject to DWT on dividends received from us if such shareholder is beneficially entitled to the dividend and is either:

- a person (not being a company) resident for tax purposes in a Relevant Territory (including the United States) and is neither resident nor ordinarily resident in Ireland (Relevant Territories for DWT purposes include the following: Albania, Armenia, Australia, Austria, Bahrain, Belarus, Belgium, Bosnia & Herzegovina, Botswana, Bulgaria, Canada, Chile, China, Croatia, Cyprus, Czech Republic, Denmark, Egypt, Estonia, Ethiopia, Finland, France, Georgia, Germany, Ghana, Greece, Hong Kong, Hungary, Iceland, India, Israel, Italy, Japan, Kazakhstan, Kenya, Korea, Kosovo, Kuwait, Latvia, Lithuania, Liechtenstein, Luxembourg, Macedonia, Malaysia, Malta, Mexico, Moldova, Montenegro, Morocco, Netherlands, New Zealand, Norway, Oman, Pakistan, Panama, Poland, Portugal, Qatar, Romania, Russia, Saudi Arabia, Serbia, Singapore, Slovak Republic, Slovenia, South Africa, Spain, Sweden, Switzerland, Thailand, The Republic Of Turkey, Ukraine, United Arab Emirates, United Kingdom, United States, Uzbekistan, Vietnam and Zambia);

- a company which is not resident for tax purposes in Ireland but is resident for tax purposes in a Relevant Territory, provided such company is not under the control, whether directly or indirectly, of a person or persons who is or are resident in Ireland;

- a company, which is not resident for tax purposes in Ireland, that is controlled, directly or indirectly, by persons resident in a Relevant Territory and who is or are (as the case may be) not controlled by, directly or indirectly, persons who are not resident in a Relevant Territory;

- a company, which is not resident for tax purposes in Ireland, whose principal class of shares (or those of its 75% direct or indirect parent) is substantially and regularly traded on a stock exchange in Ireland, on a recognized stock exchange in a Relevant Territory or on such other stock exchange approved by the Irish Minister for Finance; or

- a company, which is not resident for tax purposes in Ireland, that is wholly-owned, directly or indirectly, by two or more companies where the principal class of shares of each of such companies is substantially and regularly traded on a stock exchange in Ireland, on a recognized stock exchange in a Relevant Territory or on such other stock exchange approved by the Irish Minister for Finance,

and provided, in all cases noted above, we have received from the shareholder, where required, the relevant DWT Form(s) prior to the payment of the dividend and such DWT Form(s) remain valid.

For non-Irish resident shareholders that cannot avail themselves of one of Ireland's domestic law exemptions from DWT, it may be possible for such shareholders to rely on the provisions of a double tax treaty to which Ireland is party to reduce the rate of DWT.

Our shareholders that do not fall within any of the categories specifically referred to above may nonetheless fall within other exemptions from DWT (subject if required to certain administrative obligations being satisfied). If any shareholders are exempt from DWT, but receive dividends subject to DWT, such shareholders may apply for refunds of such DWT from the Revenue Commissioners of Ireland.

Income Tax on Dividends Paid on our Ordinary Shares

Irish income tax may arise for certain persons in respect of dividends received from Irish resident companies. A shareholder that is not resident or, in the case of individuals, ordinarily resident in Ireland and that is entitled to an exemption from DWT generally has no liability to Irish income tax or the universal social charge on a dividend received from us. An exception to this position may apply where such shareholder holds our ordinary shares through a branch or agency in Ireland through which a trade is carried on.

A shareholder that is not resident or ordinarily resident in Ireland and that is not entitled to an exemption from DWT generally has no additional Irish income tax liability or a liability to the universal social charge. The DWT deducted by us discharges the liability to income tax. An exception to this position may apply where the shareholder holds our ordinary shares through a branch or agency in Ireland through which a trade is carried on.

Capital Acquisitions Tax

Irish capital acquisitions tax, or CAT, comprises principally gift tax and inheritance tax. CAT could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares are regarded as property situated in Ireland for Irish CAT purposes as our share register must be held in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

CAT is levied at a rate of 33% above certain tax-free thresholds. The appropriate tax-free threshold is dependent upon (i) the relationship between the donor and the donee, and (ii) the aggregation of the values of previous taxable gifts and taxable inheritances received by the donee from persons within the same group threshold. Gifts and inheritances passing between spouses of the same marriage or civil partners of the same civil partnership are exempt from CAT. Children have a tax free threshold of €400,000 in respect of taxable gifts or inheritances received from their parents. Our shareholders should consult their own tax advisors as to whether CAT is creditable or deductible in computing any domestic tax liabilities.

There is also a "small gift exemption" from CAT whereby the first €3,000 of the taxable value of all taxable gifts taken by a donee from any one donor, in each calendar year, is exempt from CAT and is also excluded from any future aggregation. This exemption does not apply to an inheritance.

THE IRISH TAX CONSIDERATIONS SUMMARIZED ABOVE ARE FOR GENERAL INFORMATION ONLY. HOLDERS OF OUR ORDINARY SHARES SHOULD CONSULT WITH THEIR TAX ADVISORS REGARDING THE TAX CONSEQUENCES IN IRELAND, INCLUDING RELATING TO THE ACQUISITION, OWNERSHIP AND DISPOSAL OF OUR ORDINARY SHARES.

F. Dividends and Paying Agents

Not applicable.

G. Statement by Experts

Not applicable.

H. Documents on Display

We are subject to the informational requirements of the Exchange Act. Accordingly, we are required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. The SEC maintains an Internet site at www.sec.gov that contains reports, proxy and information statements and other information we have filed electronically with the SEC. As a foreign private issuer, we are exempt under the Exchange Act from, among other things, the rules prescribing the furnishing and content of proxy statements, and our executive officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act.

Additionally, pursuant to Irish law, copies of this Annual Report and any information which has been or may be incorporated by reference in this Annual Report, shall be available for inspection by any shareholder of record without charge at all reasonable times at our principal place of business at Joshua Dawson House, Dawson Street, Dublin 2, D02 RY95, Ireland.

We also make available on our website, free of charge, our Annual Report and the text of our reports on Form 6-K, including any amendments to these reports, as well as certain other SEC filings, as soon as reasonably practicable after they are electronically filed with or furnished to the SEC. Our website address is www.ghres.com. The reference to our website is an inactive textual reference only, and information contained therein or connected thereto is not incorporated into this Annual Report.

I. Subsidiary Information

For information on our subsidiary, see "Item 4. Information on the Company—C. Organizational Structure," and Exhibit 8.1 to this Annual Report.

J. Annual Report to Security Holders

If we are required to provide an annual report to security holders in response to the requirements of Form 6-K, we will submit the annual report to security holders in electronic format in accordance with the EDGAR Filer Manual.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Foreign Exchange Risk

We operate internationally and are exposed to foreign exchange risk arising from various currency exposures, primarily with respect to U.S. dollar, euro and pounds sterling.

Transaction exposure arises because the amount of local currency paid or received in transactions denominated in foreign currencies may vary due to changes in exchange rates. Foreign exchange risk arises from:

- forecast expenses denominated in a currency other than the entity's functional currency; and
- recognized assets and liabilities denominated in a currency other than the entity's functional currency.

We are exposed to foreign exchange risk in respect of cash and cash equivalents which are held in a currency other than the entity's functional currency. We are also exposed to foreign exchange risk in respect of our subsidiary as its functional currency is euro. Accordingly, future changes in exchange rates will expose the Group to currency gains or losses that will impact the reported amounts of income and expenses and the impact could be material.

For the year ended December 31, 2025, we recognized a foreign exchange gain of $1.8 million, compared to a foreign exchange gain of $2.1 million for the year ended December 31, 2024. The foreign exchange gain primarily relates to the Group's foreign currency holdings of cash, cash equivalents and other financial assets and the associated strengthening or weakening of those foreign currencies throughout the year. In the year ended December 31, 2024, the foreign exchange gain primarily related to the U.S. dollar cash and other financial assets holding of our subsidiary and the associated strengthening of the U.S. dollar. Movement in foreign exchange rates could positively or negatively impact us and the effect could be material. At December 31, 2025, if foreign currency exchange rates had strengthened/weakened by 10% against the U.S. dollar, with all other variables held constant, the loss before tax for the year would have been $8.0 million higher/lower (2024: $2.3 million higher/lower).

We do not believe there is currently a need to enter into specific contracts to reduce the exposure to changes in foreign exchange rates, such as by entering into options or forward contracts. We may in the future consider using options or forward contracts to manage currency transaction exposures.

Credit Risk

Credit risk is the risk that a counterparty will not meet its obligations under a financial instrument or customer contract, leading to a financial loss. We are primarily exposed to credit risk on our cash and cash equivalents and marketable securities. Our cash balance is maintained with well-established, highly rated financial institutions. As of December 31, 2025, the cash balance is held at three banks that have a minimum S&P's credit rating of A-. As of December 31, 2025, we hold investments in investment grade bonds and in money market funds ("the Portfolio"). These investments are exposed to credit risk in the event of default of the counterparty. We do not invest in equity instruments or derivatives and none of the bonds are individually above 3% of the value of the Portfolio.

Interest Rate Risk

Interest rate risk is the risk of a change in the price of a financial instrument due to fluctuations in interest rates, leading to a financial loss. We are exposed to interest rate risk on our marketable securities. The value of our marketable securities would decrease in the short term in the event of an interest rate increase in alternative investments.

As of December 31, 2025, if interest rates had increased / decreased by 50 basis points, with all other variables held constant, the Group's total comprehensive loss would have been $0.1 million higher / lower (2024: $0.3 million higher / lower), due to the movement in the fair value of the Group's marketable securities.

Liquidity Risk

Liquidity risk is the risk that we may not be able to generate sufficient cash resources to settle our obligations in full as they fall due or can do so only on terms that are materially disadvantageous. Prudent liquidity risk management implies maintaining sufficient cash to cover working capital requirements. Cash is monitored by management.

Funding and liquidity risks are reviewed regularly by our Board of Directors and management. We fund our capital requirements through capital raising.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt Securities

Not applicable.

B. Warrants and Rights

Not applicable.

C. Other Securities

Not applicable.

D. American Depositary Shares

Not applicable.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

Not applicable.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

A. Disclosure Controls and Procedures

The Company's management, with the participation of the Company's Chief Executive Officer and Vice President, Finance, has evaluated the effectiveness of the Company's disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e)) as of December 31, 2025. Based on such evaluations, our Chief Executive Officer and Vice President, Finance, have concluded that these disclosure controls and procedures were effective as of the end of the period covered by this Annual Report. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives.

B. Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. This rule defines internal control over financial reporting as a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer and effected by the board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with IFRS Accounting Standards as adopted by the International Accounting Standards Board (IASB) and includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with IFRS Accounting Standards, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements., and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2025. This assessment was performed under the direction and supervision of our Chief Executive Officer and our Vice President, Finance, and based on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO.

Based on such evaluation, management, including our Chief Executive Officer and Vice President, Finance concluded that, our internal control over financial reporting was effective as of December 31, 2025.

C. Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of the Company's registered public accounting firm because we are an emerging growth company under the JOBS Act and as such, we are exempted from such attestation requirement.

D. Changes in Internal Control Over Financial Reporting

There were no changes to internal control over financial reporting (as defined in Exchange Act Rule 13a-15(f)) during the fiscal year ended December 31, 2025, that would have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16. [RESERVED]

A. Audit Committee Financial Expert

Our Board of Directors has determined that each of Dermot Hanley, Michael Forer and Duncan Moore is considered an "audit committee financial expert" as defined by the SEC. Our Board of Directors has determined that each of Dermot Hanley, Michael Forer and Duncan Moore satisfies the "independence" requirements set forth in Rule 10A-3 under the Exchange Act.

B. Code Of Ethics

We have adopted a Code of Business Conduct and Ethics, or the Code of Ethics, that is applicable to all of our employees, executive officers and directors. The Code of Ethics is available on our website www.ghres.com. The audit committee of our Board of Directors is responsible for overseeing the Code of Ethics and is required to approve any waivers of the Code of Ethics for employees, executive officers and directors. We expect that any substantive amendments to the Code of Ethics will be disclosed on our website and we will also publicly disclose any waivers for executive officers or directors of its requirements on our website within four business days following such waiver. For the year ended December 31, 2025, we did not grant any waivers of the Code of Ethics for executive officers or directors.

C. Principal Accountant Fees And Services

For the years ended December 31, 2025 and 2024, PricewaterhouseCoopers, the Irish member firm of PricewaterhouseCoopers International Limited, acted as our independent registered public accounting firm.

"PwC entities" means PricewaterhouseCoopers, the auditor of the Company, as well as all of the foreign entities belonging to the PwC network of individual firms.

The following table summarizes the approximate fees for services rendered by PwC entities for the years ended December 31, 2025 and 2024:

	For the Years Ended December 31,	
	2025	2024
	(In USD thousands)	
Audit fees	1,086	717
Total Fees	1,086	717

Audit fees include the standard audit work performed each fiscal year necessary to allow the auditor to issue an opinion on our consolidated financial statements and to issue a report on our local statutory financial statements. Audit fees also include services that can be provided only by the external auditor such as reviews of quarterly financial results and consents and comfort letters and any other audit services required for SEC or other regulatory filings.

Pre-Approval Policies and Procedures

In accordance with the requirements of the Sarbanes-Oxley Act and rules issued by the SEC, our audit committee reviews and pre-approves all audit and permitted non-audit services performed by our independent registered public accounting firm. The procedures require that all proposed future engagements of our independent registered public accounting firm for audit and permitted non-audit work are submitted to our audit committee for approval prior to the beginning of any such service. In accordance with this policy, all services performed by, and all fees paid to PwC entities after our initial public offering were approved by our audit committee, following its formation.

D. Exemptions From The Listing Standards For Audit Committees

None.

E. Purchases Of Equity Securities By The Issuer And Affiliated Purchasers

During the year ended December 31, 2025, no purchases of our equity securities were made by or on behalf of GH Research PLC or any "affiliated purchaser" as such term is defined in Rule 10b-18 under the Exchange Act.

F. Change In Registrant's Certifying Accountant

None.

G. Corporate Governance

As a "foreign private issuer," as defined by the SEC, we are permitted, consistent with Nasdaq Stock Market Rule 5615(a)(3), to follow home country corporate governance practices, instead of certain corporate governance standards required by Nasdaq for U.S. companies. Accordingly, we follow Irish corporate governance rules in lieu of certain of Nasdaq's corporate governance requirements. A foreign private issuer that elects to follow a home country practice instead of any of any such Nasdaq requirements must submit to Nasdaq, in advance, a written statement from an independent counsel in such issuer's home country certifying that the issuer's practices are not prohibited by the home country's laws. We provided Nasdaq with such a letter of non-compliance with respect to:

- The Rule requiring maintaining a majority of independent directors (Rule 5605(b)(1)). Although we currently maintain a majority of independent directors, we may follow Irish law and practice in the future, under which we are not required to appoint a majority of independent directors.

- The Rule requiring that our independent directors have regularly scheduled meetings at which only independent directors are present (Rule 5605(b)(2)). Instead, we follow Irish law according to which independent directors are not required to hold executive sessions.

- The Rule regarding independent director oversight of director nominations process for directors (Rule 5605(e)). Instead, we follow Irish law and practice according to which our Board of Directors recommends directors for election/re-election by our shareholders.

- The requirement to obtain shareholder approval for the establishment or amendment of certain equity based compensation plans (Rule 5635(c)), an issuance that will result in a change of control of the company (Rule 5635(b)), certain transactions other than a public offering involving issuances of a 20% or more interest in the company (Rule 5635(d)) and certain acquisitions of the stock or assets of another company (Rule 5635(a)). Instead, we follow Irish law and practice in approving such procedures, according to which Board approval may suffice in certain circumstances, depending on the extent existing general authorities to issue shares are in place in accordance with our Constitution.

- The Rule requiring a compensation committee consisting of at least two independent directors (Rule 5605(d)(2)). We have a compensation committee, which we refer to as the remuneration committee, and to preserve greater flexibility over whom we may appoint to the remuneration committee, we instead follow Irish law which does not require us to have an independent compensation committee.

- The Rule requiring a quorum of $33^{1/3}$% at any meeting of shareholders (Rule 5620(c)). Instead, we follow the provisions of our Constitution which require a quorum of 25%.

See “Item 6. Directors, Senior Management and Employees” and “Item 10. Additional Information—B. Memorandum and Articles of Association” for further information.

H. Mine Safety Disclosure

Not applicable.

I. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections

Not applicable.

J. Insider Trading Policies

Our Board of Directors has adopted an insider trading policy applicable to our directors, officers, employees, and other covered persons, and have implemented processes for the company, that we believe are reasonably designed to promote compliance with applicable insider trading laws, rules and regulations and Nasdaq listing standards. Our insider trading policy is filed as Exhibit 11.1 to this Annual Report.

K. Cybersecurity

Cybersecurity risk management is an integral part of our overall enterprise risk management strategy. As a growing company and given the ever-evolving nature of cybersecurity risks, we regularly review and seek to improve our strategies for addressing cybersecurity risks and threats. Our approach to cybersecurity risk management involves identifying, monitoring, assessing, and responding to cybersecurity threats and incidents, facilitating coordination across different departments of the Company, and escalating issues within management and to the Board of Directors, as appropriate.

We engage a third-party IT service provider to assist us with implementation and operation of technical controls designed to identify, assess, manage and mitigate cybersecurity risks. This includes management of endpoints, patches, user access and incidents, as well as IT change management. Cybersecurity awareness training is also provided to employees on an ongoing basis. We also have processes in place to oversee and identify risks from cybersecurity threats associated with our use of third-party vendors and service providers.

Management is responsible for identifying, assessing and managing material cybersecurity risks on an ongoing basis. Cybersecurity risk management is under the direction of our co-founder and Managing Director, Ireland who has maintained responsibility for IT and cybersecurity since the establishment of the Company. He is assisted in this role by our IT Director, Finance team, professional IT consultants that we engage from time to time and our third-party IT service provider. Management receives updates and reports from our third-party IT service provider regarding cybersecurity matters on a regular basis. Management provides quarterly updates to the audit committee regarding IT and cybersecurity risks and mitigation strategies in place to address them.

Our Board of Directors has ultimate oversight responsibility for enterprise risk management, including cybersecurity risk management, and delegates cybersecurity risk management oversight to the audit committee. The audit committee meets on a quarterly basis and is responsible for reviewing the Company's approach and practices with respect to risk assessment and management, which includes cybersecurity risks. On at least an annual basis, management provides an update to the Board of Directors on cybersecurity risk. Additionally, management would follow a risk-based escalation process to notify the audit committee and Board of Directors outside of the cycle of regular updates if they identify an emerging risk or material issue. As part of such process, any material cybersecurity incidents would be escalated by management to the Board of Directors.

Despite our efforts, we cannot eliminate all risks from cybersecurity threats. We cannot provide assurances that we have not experienced an undetected cybersecurity incident, and we cannot guarantee that our information technology systems include sufficient controls to prevent future cybersecurity incidents. For more information about these risks and how they have impacted our Company, please see "Item 3. Key Information—D. Risk Factors—Risks Related to Employee Matters, Managing Our Business and Operations—Cyber-attacks or other failures in our telecommunications or IT systems, or those of our collaborators, CROs, third-party logistics or other service providers, distributors, suppliers or other contractors or consultants, could result in information theft, data corruption and significant disruption or unavailability of our business operations".

PART III

ITEM 17. FINANCIAL STATEMENTS

We have responded to Item 18 in lieu of this item.

ITEM 18. FINANCIAL STATEMENTS

Financial Statements are filed as part of this Annual Report, beginning on page F-1.

ITEM 19. EXHIBITS

The following documents are filed as part of this Annual Report.

EXHIBIT INDEX

Exhibit No.	Description	Incorporation by Reference			
		Form	File No.	Exhibit No.	Filing Date
1.1	Constitution of GH Research PLC	20-F	001-40530	1.1	March 9, 2023
2.1*	Description of Securities				
4.1§*	GH Research PLC Share Option Plan, as amended May 15, 2025				
8.1	List of subsidiaries	F-1	333-256796	21.1	June 4, 2021
11.1	Insider Trading Policy	20-F	001-40530	11.1	February 27, 2025
12.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
12.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
13.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
13.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
15.1*	Consent of Independent Registered Public Accounting Firm				
97.1	Policy for the Recovery of Erroneously Awarded Compensation	20-F	001-40530	97.1	February 27, 2025
101.INS	Inline XBRL Instance Document				
101.SCH	Inline XBRL Taxonomy Extension Schema Document				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)				

* Filed herewith.

§ Management contract, compensatory plan or arrangement.

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this Annual Report on its behalf.

GH Research PLC

Date: March 5, 2026

By: /s/ Velichka Valcheva
Name: Velichka Valcheva
Title: Chief Executive Officer

By: /s/ Julie Ryan
Name: Julie Ryan
Title: Vice President, Finance

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of GH Research PLC

Opinion on the Financial Statements

We have audited the accompanying consolidated statements of financial position of GH Research PLC and its subsidiary (the "Company") as of December 31, 2025 and 2024, and the related consolidated statements of comprehensive loss, changes in equity, and cash flows for each of the three years in the period ended December 31, 2025, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2025 in conformity with IFRS Accounting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers
Dublin, Ireland
March 5, 2026

We have served as the Company's auditor since 2021.

GH RESEARCH PLC
Consolidated statement of comprehensive loss

	Note	Year ended December 31, 2025 $'000	2024 $'000	2023 $'000
Operating expenses				
Research and development	3	(38,765)	(35,016)	(29,821)
General and administration	3	(21,953)	(15,296)	(11,401)
Loss from operations		**(60,718)**	**(50,312)**	**(41,222)**
Finance income	5	11,128	9,873	8,978
Finance expense	5	(463)	(717)	(723)
Movement of expected credit loss	10	42	66	1
Foreign exchange gain/(loss)	19	1,753	2,129	(2,621)
Total other income		**12,460**	**11,351**	**5,635**
Loss before tax		**(48,258)**	**(38,961)**	**(35,587)**
Tax charge/(credit)	6	—	—	—
Loss for the year		**(48,258)**	**(38,961)**	**(35,587)**
Other comprehensive (expense)/income				
Items that may be reclassified to profit or loss				
Fair value movement on marketable securities	10	(127)	(173)	(95)
Currency translation adjustment		785	(2,054)	2,528
Total comprehensive loss for the year		**(47,600)**	**(41,188)**	**(33,154)**
Attributable to owners:				
Loss for the year		(48,258)	(38,961)	(35,587)
Total comprehensive loss for the year		(47,600)	(41,188)	(33,154)
Loss per share				
Basic and diluted loss per share (in USD)	21	(0.79)	(0.75)	(0.68)

The accompanying notes to the consolidated financial statements are an integral part of these consolidated financial statements.

GH RESEARCH PLC
Consolidated statement of financial position

	Note	At December 31, 2025 $'000	2024 $'000
ASSETS			
Current assets			
Cash and cash equivalents	8	246,251	100,791
Other financial assets	8	-	19,387
Marketable securities	10	34,457	29,146
Other current assets	9	5,268	4,901
Total current assets		**285,976**	**154,225**
Non-current assets			
Marketable securities	10	-	33,300
Property, plant and equipment	11	620	748
Other non-current assets	12	1,634	-
Total non-current assets		**2,254**	**34,048**
Total assets		**288,230**	**188,273**
LIABILITIES AND EQUITY			
Current liabilities			
Trade payables	13	3,773	3,741
Lease liability	15	365	255
Other current liabilities	14	4,242	4,957
Total current liabilities		**8,380**	**8,953**
Non-current liabilities			
Lease liability	15	147	369
Total non-current liabilities		147	369
Total liabilities		**8,527**	**9,322**
Equity attributable to owners			
Share capital	16	1,551	1,301
Additional paid-in capital	16	431,061	291,463
Other reserves	16	13,292	5,194
Foreign currency translation reserve	16	(11,776)	(12,561)
Accumulated deficit		(154,425)	(106,446)
Total equity		**279,703**	**178,951**
Total liabilities and equity		**288,230**	**188,273**

The accompanying notes to the consolidated financial statements are an integral part of these consolidated financial statements.

GH RESEARCH PLC
Consolidated statement of changes in equity

	Attributable to owners					
	Share capital $'000	Additional paid-in capital $'000	Other reserves $'000	Foreign currency translation reserve $'000	Accumulated deficit $'000	Total $'000
	Note 16	Note 16	Note 16	Note 16		
At January 1, 2023	**1,301**	**291,448**	**2,595**	**(13,035)**	**(32,493)**	**249,816**
Loss for the year	—	—	—	—	(35,587)	(35,587)
Other comprehensive (loss)/income	—	—	(95)	2,528	—	2,433
Total comprehensive (loss)/income for the year	**—**	**—**	**(95)**	**2,528**	**(35,587)**	**(33,154)**
Share-based compensation expense	—	—	2,291	—	—	2,291
Share option exercises	—	15	(140)	—	140	15
Total transactions with owners	**—**	**15**	**2,151**	**—**	**140**	**2,306**
At December 31, 2023	**1,301**	**291,463**	**4,651**	**(10,507)**	**(67,940)**	**218,968**
At January 1, 2024	**1,301**	**291,463**	**4,651**	**(10,507)**	**(67,940)**	**218,968**
Loss for the year	—	—	—	—	(38,961)	(38,961)
Other comprehensive loss	—	—	(173)	(2,054)	—	(2,227)
Total comprehensive loss for the year	**—**	**—**	**(173)**	**(2,054)**	**(38,961)**	**(41,188)**
Share-based compensation expense	—	—	1,171	—	—	1,171
Transfer of share options	—	—	(455)	—	455	—
Total transactions with owners	**—**	**—**	**716**	**—**	**455**	**1,171**
At December 31, 2024	**1,301**	**291,463**	**5,194**	**(12,561)**	**(106,446)**	**178,951**
At January 1, 2025	**1,301**	**291,463**	**5,194**	**(12,561)**	**(106,446)**	**178,951**
Loss for the year	—	—	—	—	(48,258)	(48,258)
Other comprehensive (loss)/income	—	—	(127)	785	—	658
Total comprehensive (loss)/income for the year	**—**	**—**	**(127)**	**785**	**(48,258)**	**(47,600)**
Share-based compensation expense	—	—	8,504	—	—	8,504
Transfer of share options	—	—	(269)	—	269	—
Share option exercises	—	—	(10)	—	10	—
Issue of share capital	250	139,598	—	—	—	139,848
Total transactions with owners	**250**	**139,598**	**8,225**	**—**	**279**	**148,352**
At December 31, 2025	**1,551**	**431,061**	**13,292**	**(11,776)**	**(154,425)**	**279,703**

The accompanying notes to the consolidated financial statements are an integral part of these consolidated financial statements.

GH RESEARCH PLC
Consolidated statement of cash flows

	Note	Year ended December 31, 2025 $'000	2024 $'000	2023 $'000
Cash flows from operating activities				
Loss for the year		**(48,258)**	**(38,961)**	**(35,587)**
Depreciation	11	335	315	315
Share-based compensation expense	18	8,504	1,171	2,291
Finance income	5	(11,128)	(9,873)	(8,978)
Finance expense	5	463	717	723
Movement of expected credit loss	10	(42)	(66)	(1)
Foreign exchange (gain)/loss	19	(1,753)	(2,129)	2,621
Movement in working capital		(3,094)	188	1,645
Cash flows used in operating activities		**(54,973)**	**(48,638)**	**(36,971)**
Finance expense paid		(639)	(723)	(648)
Finance income received		12,060	7,076	4,283
Net cash used in operating activities		**(43,552)**	**(42,285)**	**(33,336)**
Cash flows from/(used in) investing activities				
Purchase of property, plant and equipment	11	(121)	(49)	(100)
Purchase of other financial assets	8	—	—	(54,000)
Proceeds from sale of other financial asset	8	19,585	38,000	—
Proceeds from redemptions and disposals of marketable securities	10	26,708	27,184	—
Cash flows from/(used in) investing activities		**46,172**	**65,135**	**(54,100)**
Cash flows from/(used in) financing activities				
Payment of lease liability	15	(197)	(304)	(219)
Proceeds from equity public offering	16	150,000	—	—
Transaction costs from equity public offering	16	(10,152)	—	—
Proceeds from share issuances	16	—	—	15
Net cash flows from/(used in) financing activities		**139,651**	**(304)**	**(204)**
Net increase/(decrease) in cash and cash equivalents		**142,271**	**22,546**	**(87,640)**
Cash and cash equivalents at the beginning of the year		100,791	78,420	165,955
Impact of foreign exchange on cash and cash equivalents		3,189	(175)	105
Cash and cash equivalents at the end of the year		**246,251**	**100,791**	**78,420**

The accompanying notes to the consolidated financial statements are an integral part of these consolidated financial statements.

GH RESEARCH PLC
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

1. Corporate information

GH Research PLC (the "Company") was incorporated on March 29, 2021. The registered office of the Company is located at Joshua Dawson House, Dawson Street, Dublin 2, Ireland. The Company controls one wholly-owned subsidiary: GH Research Ireland Limited, which was incorporated in Dublin, Ireland on October 16, 2018. The Company and its subsidiary form the GH Research Group (the "Group" or "GH Research").

The Group is a clinical-stage biopharmaceutical company dedicated to transforming the lives of patients by developing a practice-changing treatment in depression. Its initial focus is on developing the novel and proprietary mebufotenin therapies for the treatment of patients with Treatment Resistant Depression, or TRD. Its portfolio currently includes GH001, a proprietary inhalable mebufotenin product candidate and GH002, a proprietary intravenous mebufotenin product candidate.

These consolidated financial statements were presented to the Board of Directors and approved by them for issue on March 5, 2026.

2. Basis of preparation, significant judgments, and accounting policies

Basis of preparation

Compliance with IFRS Accounting Standards

The consolidated financial statements for the year ended December 31, 2025, have been prepared in accordance with IFRS Accounting Standards as adopted by the International Accounting Standards Board ("IASB"). These consolidated financial statements are presented in U.S. dollar ("USD" or "$"), which is the Company's functional currency and the Group's presentation currency. The financial statements have been prepared under the historical cost convention aside from the measurement at fair value of all investments in money market funds and marketable securities and the measurement of share-based payments at initial date of award.

The financial information presented in this report does not represent full statutory accounts as defined by the Companies Act 2014. The statutory accounts of GH Research PLC for the year ended December 31, 2025, are expected to be filed with the Companies Registration Office by November 26, 2026.

New and amended IFRS Accounting Standards

There are no new IFRS Accounting Standards, amendments to standards or interpretations that are mandatory for the financial year beginning on January 1, 2025, that are relevant to the Group and that have had any material impact on the consolidated financial statements. The review of the impact of new standards on the Group's financial statements which are not yet effective and which have not been early adopted by the Group is ongoing. This includes the recently issued IFRS 18 "Presentation and Disclosure in Financial Statements". IFRS 18 will replace IAS 1 "Presentation of financial statements", introducing new requirements that will help to achieve comparability of the financial performance of similar entities and provide more relevant information and transparency to users. Management is currently assessing the detailed implications of applying the new standard on the Group's financial statements.

Going concern basis

GH Research is a clinical-stage biopharmaceutical company developing innovative therapeutics. The Group is exposed to all risks inherent in establishing and developing its business, including the substantial uncertainty that current projects will succeed. Research and development expenses have been incurred from the start of the Group's activities, generating negative cash flows from operating activities since formation.

Since its incorporation, the Group has funded its growth through capital increases. The Group has no bank loans or other debt outstanding, except lease liabilities, as of December 31, 2025. As a result, the Group is not exposed to liquidity risk through requests for early repayment of loans.

As of December 31, 2025, the Group's cash and cash equivalents amounted to $246.3 million (December 31, 2024: $100.8 million). The Group also held marketable securities of $34.5 million and other financial assets of $nil as of December 31, 2025 (December 31, 2024: marketable securities of $62.4 million and other financial assets of $19.4 million). The Group's marketable securities are quoted in active markets and are an additional source of liquidity.

The Board of Directors believes that the Group has sufficient financial resources available to cover its planned cash outflows for at least the next twelve months from the date of issuance of these consolidated financial statements. The Group, therefore, continues to adopt the going concern basis in preparing its consolidated financial statements.

Use of estimates and judgments

The preparation of the consolidated financial statements requires management to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets and liabilities, income and expense. Actual results may differ from these estimates.

In preparing these consolidated financial statements, the significant judgments made by management in applying the Group's accounting policies and the key sources of estimation uncertainty are as follows:

Functional currency

As explained in this Note and in Note 19, the functional currency of the subsidiary, GH Research Ireland Limited, is euro. Judgment was applied in the determination that euro was the appropriate functional currency of the subsidiary. The principal consideration supporting this decision was made by reference to the current activities the subsidiary undertakes which is the execution of clinical trials for which the costs are primarily in euro. Judgment was also applied in the determination that the U.S. dollar is the functional currency of the parent company with the principal considerations being that most of the expenses incurred and all funding raised are in U.S. dollars.

Share-based compensation expense

In preparing the share based-compensation expense in prior periods, the expected volatility assumption was based on selected volatility determined by median values observed among other comparable public companies.

In preparing the share-based compensation expense for these consolidated financial statements, the Group has used a blended rate taking into account its own historical volatility alongside other comparable public companies. This change has been made due to the historical share price information now available for the Group. Judgment has been applied, for all periods presented, in the selection of comparable public companies and of the relevant period of observation used to determine the values.

Prepaid and Accrued Research and Development Expenses

The Group has entered into various research and development contracts with research institutions and other companies. As part of preparing the consolidated financial statements, the Group is required to estimate the prepaid and accrued research and development expenses. This process involves reviewing open contracts, communicating with our personnel to identify services which have been performed on the Group's behalf and estimating the level of service which has been performed and the associated cost relating to that service when the Group has not yet been invoiced or otherwise notified of actual costs. Estimates of our prepaid and accrued research and development expenses are made at each balance sheet date based on the facts and circumstances known at the time. The estimate of prepaid and accrued research and development expenses is dependent, in part, upon the receipt of timely and accurate information from CROs and other third party-service providers. Although the Group does not expect the estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed may vary and may result in reporting that is too high or too low in any particular period.

Deferred tax balances and the valuation of tax operating losses

During the period from incorporation of GH Research Ireland Limited to December 31, 2025, the Group has incurred losses, which are a potential benefit in the event that the Group reports a taxable profit in the future. In preparing these financial statements, the Group has assessed that the likelihood of a taxable profit is currently not sufficiently certain for these potential benefits to be recognized as a deferred tax asset. This assessment is based on the status of the research into the Group's principal investigational product and the significant challenges that remain before operating profits can be assured (refer to Note 7, "Deferred income taxes").

Research and development tax credits

As a Group, we carry out extensive research and development activities and have assessed whether those activities qualify for a credit under the Irish research and development tax legislation. Qualifying expenditures largely comprise employment costs for research staff for which an estimate of time spent directly or indirectly supporting the pursuit of research and development activities is made, consumables and outsourced contract research organization costs. Judgment is made by management in determining the expenditure which is considered qualifying.

During the year ended December 31, 2025, $3.4 million relating to the research and development tax credit has been recognized (2024: $2.6 million). Included in this amount is an estimate of the claim for the year ended December 31, 2025 (2024: estimate relating to a component of the claim for the year ended December 31, 2024, as reasonable assurance on the remaining components of that claim had not been achieved at that date).

A portion of the research and development tax credit claimed remains unrecognized at December 31, 2025, as management has assessed that some uncertainty remains and therefore, reasonable assurance has not been achieved. Reasonable assurance is achieved using internal experience, judgment and assistance from our professional advisors. If the portion of the research and development tax credit which remains unrecognized at December 31, 2025, increased or decreased by 5%, this would not have a material impact on the financial statements.

Material accounting policies

Consolidation

The consolidated financial statements incorporate the financial statements of the Company and its subsidiary, GH Research Ireland Limited. Subsidiaries are all entities over which the Company has control. Control is achieved when the Company has power over an entity, is exposed to or has rights to variable returns from its involvement with the entity and has the ability to affect returns through its power over the entity. Subsidiaries are fully consolidated from the date on which control is transferred to the Company. They are deconsolidated from the date that control ceases. All intercompany transactions have been eliminated.

Foreign currency translation

The functional currency of the Company is the U.S. dollar given it is listed on Nasdaq and its fundraising activities and most of its expenses incurred are in U.S. dollars. The functional currency of its subsidiary, GH Research Ireland Limited, is euro due to its expenses being mainly incurred in euro. These consolidated financial statements are presented in U.S. dollar which is the Group's presentation currency.

Items included in the financial statements of the Company's subsidiary are measured using the currency of the primary economic environment in which the entity operates, which is the euro.

Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Monetary assets and liabilities denominated in foreign currencies are retranslated at the consolidated statement of financial position date. On consolidation, the subsidiary's assets and liabilities are translated to the Group's presentation currency and the resulting foreign currency difference goes through the foreign currency translation reserve.

Cash and cash equivalents

Cash and cash equivalents represent cash held in bank current accounts with original maturities of less than three months and investments which are readily convertible to a known amount of cash and are subject to insignificant changes in value. Cash and cash equivalents are carried at amortized cost or, in the case of investments in money market funds, at fair value through profit or loss as the cash flows from these funds do not represent solely payments of principal and interest. The Group's determination of its investments as cash equivalents requires judgment, which includes assessing the ability to readily convert an instrument into cash.

The Group's cash balance is maintained with well established, highly rated financial institutions. The majority of the cash balance is held in U.S. dollars.

Financial assets

A financial asset is recognized in the statement of financial position when the Group becomes a party to its contractual provisions. At initial recognition, a financial asset is measured at fair value, adjusted for directly attributable transaction costs, with the exception of financial assets at fair value through profit and loss ("FVTPL"), which are measured at fair value and is assigned one of the following classifications for the purpose of subsequent measurement:

- financial asset at amortized cost;
- financial asset at fair value through other comprehensive income ("FVOCI"); or
- financial asset at FVTPL.

The Group determines the appropriate classification based on the contractual cash flow characteristics of the financial asset and the objective of the business model within which the financial asset is held. In determining the business model for a group of financial assets, the Group considers factors such as, how performance is evaluated and reported within the Group, the risks that impact performance and how they are managed, and the expected frequency, value and timing of sales of financial assets.

In considering the contractual cash flow characteristics of a financial asset, the Group determines whether the contractual terms give rise, on specified dates, to cash flows that are solely payments of principal and interest on the principal outstanding. In making this determination, the Group assesses whether the financial asset contains a contractual term that could change the timing or amount of the contractual cash flows such that it would not meet this condition.

Financial assets are derecognized when the Group's contractual rights to the cash flows from the financial asset expire, are extinguished or transferred to a third party.

Marketable securities are mainly comprised of investment grade bonds. At initial recognition, marketable securities are measured at fair value and subsequently at FVOCI when both of the following conditions are met:

- The asset has contractual terms that give rise to cash flows on specified dates that are solely payments of principal and interest on the principal outstanding; and
- The asset is held within a business model whose objective is achieved by both collecting contractual cash flows and selling those assets.

Purchases and sales of instruments are recognized on the trade date with gains and losses arising from changes in fair value included in Other Comprehensive Income, ("OCI"). Interest income, using the effective interest rate method, is recognized in the income statement. An impairment loss allowance is recognized for expected credit losses ("ECL"). The impairment loss allowance does not reduce the carrying value of the asset but an amount equal to the allowance is recognized in OCI, as an accumulated impairment amount, with corresponding impairment gains or losses recognized in the income statement. On derecognition, the cumulative gain or loss previously recognized in OCI is reclassified to the income statement.

Other financial assets represent money market funds with a weighted average maturity of more than 90 days and are carried at fair value through profit or loss as the cash flows from these funds do not represent solely payments of principal and interest.

Property, plant and equipment

Property, plant and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

	Estimated Useful Life
Equipment	3 years

Leases and right-of-use assets

The Group recognizes a right-of-use ("ROU") asset and a corresponding lease liability for all arrangements in which it is a lessee, except for leases with a term of 12 months or less (short-term leases) and low-value leases. Under IFRS 16, the Group recognizes a ROU asset and a lease liability at the lease commencement date at the present value of the future lease payments, discounted at the Group's incremental borrowing rate. The ROU asset is subsequently depreciated using the straight-line method over the lease term within depreciation expenses and an interest expense on lease liabilities is recognized within finance expense in the Group's consolidated statement of comprehensive loss. The interest expense is calculated based on the incremental borrowing rate of the Group.

For short-term or low value leases, the Group recognizes the lease payments as an operating expense on a straight-line basis over the term of the lease.

Trade payables and other current liabilities

Trade payables and other current liabilities are recognized initially at fair value and subsequently measured at amortized cost.

Share-based compensation expense

The fair value of options granted under the share option plan is recognized as a share-based compensation expense with a corresponding increase in equity. The total expense is recognized over the vesting period, which is the period over which all of the specified vesting conditions are to be satisfied.

Share capital and additional paid-in capital

Share capital

Share capital represents the nominal value of outstanding shares (see Note 16, "Share capital and reserves").

Additional paid-in capital

Amounts of contribution in excess of nominal value are accounted for as additional paid-in capital. Incremental costs directly attributable to equity transactions such as the issue of new capital shares are shown in equity as a deduction, net of tax, from the proceeds within additional paid-in capital. Transaction costs that relate to equity and non-equity transactions are allocated to those transactions using a basis of allocation that is rational and consistent with similar transactions. If the equity instruments are not subsequently issued, the transaction costs would be expensed.

Research and development expenses

Research and development expenses consist of costs incurred in performing research and development activities, including salaries, share-based compensation and benefits, travel, and external costs of outside vendors engaged to conduct clinical development activities, clinical trials, technical development activities and the cost to manufacture clinical trial materials.

Research expenditure is recognized as an expense in the year in which it is incurred. Internal development expenditure is capitalized only if it meets the recognition criteria of IAS 38 "Intangible Assets". Where regulatory and other uncertainties are such that the criteria are not met, the expenditure is recognized in the statement of comprehensive loss. When certain criteria are met, the Group may capitalize and amortize on a straight-line basis over its estimated useful life, internal development expenditures. To date, the Group has not capitalized any R&D expenses.

General and administrative expenses

General and administrative expenses relate to the administration of the Group including salaries, share-based compensation and benefits, travel and external costs including legal and professional fees.

Research and development tax credits

Research and development tax credits are available to the Group under the tax laws in Ireland based on qualifying research and development spend as defined under those tax laws. Research and development tax credits are recognized at their fair value where there is reasonable assurance that the tax credits will be received and the Group will comply with all conditions attaching to them. Upon recognition, the tax credits are deducted from the relevant operating expenses amount, if the related amounts were previously expensed as incurred, or deducted in arriving at the carrying value of the related asset, if the related costs had been capitalized.

Finance income and expense

The Group's finance income and expense includes:

- Interest income on cash and cash equivalents, other financial assets and marketable securities;
- Interest expense; and
- Net gain or loss on financial assets classified at FVTPL.

Interest income or expense is recognized using the effective interest rate method. The effective interest rate is the rate that discounts estimated future cash receipts through the expected life of the financial instrument to the gross carrying value of the financial asset. Amounts received from money market funds, other than those related to the sale of units, are recognized when the right to payment is established which generally occurs on receipt of the related funds.

Current and deferred income tax

The tax expense for the financial year comprises current and deferred tax. Tax is recognized in the income statement, except to the extent that it relates to items recognized in other comprehensive income or directly in equity. In this case the related tax is recognized in other comprehensive income or directly in equity, respectively.

The current income tax charge is calculated on the basis of the tax laws enacted or substantively enacted at the balance sheet date where the Group generates taxable income. Management periodically evaluates positions taken in tax returns with respect to situations in which applicable tax regulation is subject to interpretation. It establishes provisions where appropriate on the basis of amounts expected to be paid to the tax authorities.

Taxes on income are accrued in the same financial year as the income and expenses to which they relate. Current income tax assets and liabilities for the current financial year are measured at the amount expected to be recovered from or paid to the tax authorities.

Deferred income tax assets are recognized only to the extent that it is probable that future taxable profit will be available against which the temporary differences or the unused tax losses can be utilized. Deferred income tax assets from tax credit carry-forwards are recognized to the extent that the realization of the related tax benefit through future taxable profits is probable.

Contingencies

The Group assesses the likelihood of any adverse outcomes as a contingency, including legal matters. Provisions for such contingencies are recorded where it is probable that a liability will be incurred and the amount of that loss can be reliably estimated. A contingent liability is disclosed where the existence of the obligation will only be confirmed by future events, or where the amount of the obligation cannot be measured reliably.

Segment reporting

Management considers the Group to have only a single segment: Research and Development ("R&D"). This is consistent with the way that information is reported internally within the Group for the purpose of allocating resources and assessing performance.

Loss per share

Basic loss per share is calculated by dividing the net loss attributable to shareholders by the weighted average number of shares in issue during the year.

3. Expenses by nature

The following table provides the consolidated statement of comprehensive loss classification of our expense by nature:

	Year ended December 31,		
	2025 $'000	**2024 $'000**	**2023 $'000**
Research and development			
External research and development expenses [1]	26,178	27,800	23,050
Employee expenses [2] [5]	12,587	7,216	6,771
Total research and development expenses [3]	**38,765**	**35,016**	**29,821**
General and administrative			
External costs	12,956	10,182	7,692
Employee expenses [4] [5]	8,695	4,820	3,429
Depreciation	302	294	280
Total general and administrative expenses	**21,953**	**15,296**	**11,401**
Total operating expenses	**60,718**	**50,312**	**41,222**

[1] Includes depreciation expense, see Note 11 "Property, Plant and Equipment".

[2] Included in employee expenses is share-based compensation expense of $3.9 million, $0.5 million and $1.4 million for the years ended December 31, 2025, 2024 and 2023, respectively, relating to employees in the research and development department.

[3] Depreciation and other expenses have been reclassified to external research and development expenses for all periods presented as it provides more relevant information.

[4] Included in employee expenses is share-based compensation expense of $4.6 million, $0.7 million and $0.9 million for the years ended December 31, 2025, 2024 and 2023, respectively, relating to employees in the general and administrative department.

[5] Includes termination expenses incurred.

4. Employee expenses

	Year ended December 31,		
	2025 $'000	2024 $'000	2023 $'000
Salary and related expenses	11,600	10,025	7,219
Social security costs	1,178	840	690
Share based compensation expense	8,504	1,171	2,291
	21,282	**12,036**	**10,200**

Information relating to the Share Option Plan is set out in Note 18 "Share-based compensation". During the year ended December 31, 2025, $0.6 million was recognized as an expense relating to defined contribution pension plans (2024: $0.3 million, 2023: $0.1 million).

5. Finance income and expense

	Year ended December 31,		
	2025 $'000	2024 $'000	2023 $'000
Finance income			
Finance income on cash, cash equivalents and other financial assets	2,625	2,628	1,890
Gain on cash equivalents and other financial assets at FVTPL	6,046	3,598	2,950
Interest income under effective interest rate method at FVOCI	2,457	3,647	4,138
Finance income	**11,128**	**9,873**	**8,978**
Finance expense			
Finance expense on investments	(428)	(669)	(660)
Finance expense on lease liability	(35)	(48)	(63)
Finance expense	**(463)**	**(717)**	**(723)**

6. Income tax

The Group's expected tax charge/(credit) of $nil for each year is based on the applicable tax rate in Ireland and reconciles to the actual tax charge/(credit) as follows:

	Year ended December 31,		
	2025 $'000	2024 $'000	2023 $'000
Loss before tax	**48,258**	**38,961**	**35,587**
Tax credit calculated at the domestic tax rate 12.5%	(6,032)	(4,870)	(4,448)
Tax effects of:			
Losses for which no deferred tax asset was recognized	6,029	4,027	4,200
Income taxable at a higher rate of tax	583	1,594	118
Other permanent differences	(580)	(751)	130
Tax charge/(credit)	—	—	—

7. Deferred income taxes

At December 31, 2025, the Group had unused tax losses of $179.7 million (2024: $102.8 million). Deferred tax assets have not been recognized in respect of these losses because it is not sufficiently certain that the Group will generate sufficient taxable profits to be able to utilize these loss carry-forwards.

The Group held investments in money market funds and marketable securities during the year ended December 31, 2025. The Group's net deferred tax position as of December 31, 2025, was $nil. A deferred tax liability of $0.2 million (2024: $1.1 million) has been recognized in respect of potential future liabilities arising on realisation of these investments. Offsetting this deferred tax liability, was a deferred tax asset of $0.2 million (2024: $1.1 million) in respect of losses that can be used against potential future liabilities arising on realisation of these investments.

8. Cash and cash equivalents

	Year ended December 31,	
	2025 $'000	2024 $'000
Cash at bank and in hand	30,972	28,577
Cash equivalents	215,279	72,214
	246,251	**100,791**

During the year ended December 31, 2025, proceeds of $19.6 million (2024: $38.0 million) were received from the sale of other financial assets which were used to fund operating activities of the Group.

9. Other current assets

	Year ended December 31,	
	2025 $'000	2024 $'000
Prepaid expenses	3,973	3,169
VAT receivable	137	150
Other receivables	1,158	1,582
	5,268	**4,901**

At December 31, 2025, other receivables primarily represents research and development tax receivable.

10. Marketable securities

	Year ended December 31,	
Fair value	2025 $'000	2024 $'000
At January 1	**62,446**	**88,667**
Accrued interest	2,457	3,647
Interest received	(620)	(974)
Redemptions and disposals of marketable securities	(29,741)	(28,787)
Revaluation adjustment	(85)	(107)
At December 31	**34,457**	**62,446**

Marketable securities had a fair value of $34.5 million at December 31, 2025 (2024: $62.4 million). During the year ended December 31, 2025, proceeds of $29.7 million were received from the redemption and disposal of marketable securities, which includes accrued interest. The impairment loss allowance for expected credit loss ("ECL") at the reporting date was $12 thousand (2024: $0.1 million). The overall movement through OCI is shown in the table below.

	Year ended December 31,		
	2025 $'000	**2024 $'000**	**2023 $'000**
Revaluation adjustments	(85)	(107)	(94)
Movement of ECL on assets measured at FVOCI	(42)	(66)	(1)
Movement on marketable securities through OCI	**(127)**	**(173)**	**(95)**

Marketable securities at FVOCI have stated interest rates of 0.63% to 2.60% (2024: 0.25% to 3.35%) and mature within the next year.

11. Property, plant and equipment

	Equipment $'000	**ROU Assets $'000**	**Total $'000**
Cost			
At January 1, 2024	224	1,198	1,422
Additions	49	—	49
Exchange difference	(16)	(72)	(88)
At December 31, 2024	**257**	**1,126**	**1,383**
Accumulated Depreciation			
At January 1, 2024	101	252	353
Charge for the year	68	247	315
Exchange difference	(8)	(25)	(33)
At December 31, 2024	**161**	**474**	**635**
Net Book Amount			
At December 31, 2024	**96**	**652**	**748**
Cost			
At January 1, 2025	257	1,126	1,383
Additions	121	—	121
Exchange difference	31	148	179
At December 31, 2025	**409**	**1,274**	**1,683**
Accumulated Depreciation			
At January 1, 2025	161	474	635
Charge for the year	77	258	335
Exchange difference	21	72	93
At December 31, 2025	**259**	**804**	**1,063**
Net Book Amount			
At December 31, 2025	**150**	**470**	**620**

Depreciation expense of $33 thousand (2024: $21 thousand, 2023: $35 thousand) has been charged in research and development expenses and $0.3 million (2024: $0.3 million, 2023: $0.3 million) in general and administration expenses.

12. Other non-current assets

Other non-current assets represent research and development tax credit receivable.

13. Trade payables

Trade payables primarily represents amounts incurred for the provision of manufacturing, research and consulting services and legal and professional fees, which are outstanding at the end of the year. Trade payables are due to be settled at different times within 12 months.

14. Other current liabilities

	Year ended December 31,	
	2025 $'000	2024 $'000
Accruals	3,340	3,868
Social security payable	495	385
Other liabilities	407	704
	4,242	**4,957**

Other current liabilities mainly comprise accruals for operating expenses and employee tax payable and are expected to be settled within one year.

15. Leases

During the year ended December 31, 2023, the Group entered into a lease for an office space. The right-of-use asset relating to this lease has been included in property, plant and equipment. At the lease commencement date, the right-of-use asset was recognized at the present value of the future lease payments, discounted at the Group's incremental borrowing rate which was calculated as 6%.

At December 31, 2025, the Group's lease liability was $0.5 million (2024: $0.6 million). Interest expense of $35 thousand was recognized on lease liabilities in the year ended December 31, 2025 (2024: $48 thousand). The following table sets out the maturity analysis of lease payments, on an undiscounted basis.

	Year ended December 31,	
	2025 $'000	2024 $'000
Less than one year	383	271
One to two years	153	271
Two to three years	—	135
Total undiscounted lease payable	**536**	**677**

Lease expenses for short-term leases were $30 thousand for the year ended December 31, 2025 (2024: $29 thousand, 2023: $0.1 million).

16. Share capital and reserves

Share capital

Issued and fully paid shares:

	Number of outstanding shares	Share capital $'000	Additional paid-in capital $'000
At December 31, 2023	**52,028,145**	**1,301**	**291,463**
At December 31, 2024	**52,028,145**	**1,301**	**291,463**
Share issue from public offering	10,000,000	250	139,598
Share option exercises (Note 18)	1,250	—	—
At December 31, 2025	**62,029,395**	**1,551**	**431,061**

The authorized share capital of GH Research PLC is 40,000,000,000 ordinary shares of nominal value $0.025 each as of December 31, 2025.

On February 6, 2025, the Company completed a public offering on Nasdaq in which it issued and sold an aggregate of 10,000,000 ordinary shares at $15.00 per share. The net proceeds of the public offering were $139.8 million, after deducting underwriting discounts and directly attributable transaction costs of $10.2 million.

Dividend

No dividends were declared or paid during the year (2024: $nil; 2023: $nil).

Reserves

Other reserves of $13.3 million as of December 31, 2025 (2024: $5.2 million) comprises amounts expensed in the consolidated statement of comprehensive loss in connection with awards made under the Share Option Plan (see Note 18, "Share-based compensation") and fair value movement on marketable securities (see Note 10, "Marketable securities").

Foreign currency translation reserve of $11.8 million as of December 31, 2025 (2024: $12.6 million) consists of the cumulative currency translation adjustment in respect of GH Research Ireland Limited whose functional currency is euro. The translation adjustments arise from the retranslation of the results of such operations from the average exchange rate for the year to the exchange rate at the statement of financial position date as well as the retranslation of the subsidiary's applicable assets and liabilities.

17. Contingencies

As of December 31, 2025, there were no material contingencies which required adjustment to or disclosure in the consolidated financial statements (2024: none).

18. Share-based compensation

Share Options

In June 2021, the Company adopted a share option plan referred to herein as the Share Option Plan under which grants of options are made to eligible participants. The Company initially reserved 1,202,734 ordinary shares for future issuance under the Share Option Plan, which includes ordinary shares pursuant to share-based equity awards issued to date. As of December 31, 2025, the total number of ordinary shares which may be issued under the Share Option Plan was 3,721,251 and the Company has 1,117,791 ordinary shares available for the future issuance of share-based equity awards (2024: 325,861 shares, 2023: 404,718 shares).

Under the Share Option Plan, the options may be settled only in ordinary shares of the Company. Therefore, the grants of share options under the Share Option Plan have been accounted for as equity-settled under IFRS 2. As such, the Company records a charge for the vested portion of award grants and for partially earned but non-vested portion of award grants.

During the year ended December 31, 2025, the Company granted the option to purchase 770,251 ordinary shares (2024: 1,320,120 shares, 2023: 440,719 shares), respectively, which were in line with the general terms of the Share Option Plan. Of the share options granted during the year, 494,001 were granted to members of key management of the Group (2024: 1,043,120). The terms of the 770,251 share options granted during the year ended December 31, 2025, are described below:

- 261,250 share options were granted which vest 25% on the first anniversary of the date of grant, and thereafter evenly on a monthly basis over the subsequent three years and are subject to a two-year service condition. The contractual term (expiration) of these share options is eight years from the grant date with an exercise price of the closing market price on the day prior to the grant.
- 14,001 share options were granted which vested on the date of grant and are subject to a two-year service condition. The contractual term (expiration) of these share options is seven years from the grant date with an exercise price of $0.025.[(1)]
- 495,000 share options were granted which vest 25% on the first anniversary of the date of grant, and thereafter evenly on a monthly basis over the subsequent three years. The contractual term (expiration) of these share options is seven years from the grant date with an exercise price of $0.025. [(1)]

[(1)] Includes grants to members of key management of the Group.

The following table summarizes the share option awards outstanding as of December 31, 2025, 2024 and 2023:

	Average exercise price per share in USD	Number of awards	Weighted average remaining life in years
At December 31, 2022	**15.32**	**461,596**	**7.14**
Granted	5.41	440,719	7.05
Forfeited/Expired	12.02	(104,299)	6.77
Exercised	2.05	(7,296)	5.74
At December 31, 2023	**10.35**	**790,720**	**6.57**
Granted	1.37	1,320,120	6.98
Forfeited/Expired	10.85	(241,293)	6.05
At December 31, 2024	**3.95**	**1,869,547**	**6.56**
Granted	4.12	770,251	6.74
Forfeited/Expired	11.69	(43,634)	5.65
Exercised[(1)]	0.03	(1,250)	4.83
At December 31, 2025[(2)]	**3.87**	**2,594,914**	**5.91**

[(1)] The weighted average share price of share options exercised was $10.73
[(2)] 701,582 of the awards outstanding as of December 31, 2025 were exercisable (2024: 213,243, 2023: 112,244).

The weighted average grant date fair value of awards granted during the year ended December 31, 2025 was $10.43 (2024: $8.70, 2023: $7.72) per award.

The fair values of the options granted were determined on the date of the grant using the Black-Scholes option-pricing model.

The fair values of the options granted during the years ended December 31, 2025, 2024 and 2023 were determined on the date of the grant using the following assumptions:

	Year ended December 31, 2025	Year ended December 31, 2024	Year ended December 31, 2023
Share price, in USD	7.91 – 16.49	5.80 – 14.81	5.32 – 13.15
Strike price, in USD (weighted average)	4.12	1.37	5.41
Expected volatility	83% — 93%	85% — 94%	83% — 88%
Award life (weighted average)	5.65	5.55	5.6
Expected dividends	—	—	—
Risk-free interest rate	3.66% — 4.47%	3.54% — 4.52%	3.50% — 4.77%

As explained in Note 2 “Basis of preparation, significant judgments, and accounting policies”, the expected volatility for the year ended December 31, 2025, is based on a blended rate of historical volatility observed among other comparable public companies and the Company’s own historical volatility. The expected volatility for the year ended December 31, 2024, was based on selected volatility determined by median values observed among other comparable public companies.

The award life is based on the time interval between the date of grant and the date during the life of the share option after which, when making the grant, the Company expected on average that participants would exercise their options.

As of December 31, 2025, Other Reserves within equity includes $13.1 million (December 31, 2024, $4.9 million) relating to the Group’s Share Option Plan. Balances which relate to forfeited awards which had previously vested are transferred from Other Reserves to Accumulated Deficit. The amount of expense for all awards recognized for services received during the year ended December 31, 2025 was $8.5 million (2024: $1.2 million, 2023: $2.3 million).

19. Financial risk management

Financial risk factors

The Board of Directors currently reviews the Group’s cash forecast and liquidity requirements. The Group’s activities expose it to a variety of financial risks including foreign exchange risk, credit risk, interest rate risk and liquidity risk.

Foreign exchange risk

The Group operates internationally and is exposed to foreign exchange risk arising from various currency exposures, primarily with respect to the U.S. dollar, euro and pounds sterling. Transaction exposure arises because the amount of local currency paid or received in transactions denominated in foreign currencies may vary due to changes in exchange rates. Foreign exchange risk arises from:

- forecast expenses denominated in a currency other than the entity’s functional currency; and
- recognized assets and liabilities denominated in a currency other than the entity’s functional currency.

The Group’s cash, cash equivalents and other financial assets are denominated in the following currencies:

	2025 Local Currency ‘000	2025 $’000	2024 Local Currency ‘000	2024 $’000
In USD	165,814	165,814	119,363	119,363
In Euro	56,208	66,045	723	752
In GBP	10,688	14,392	50	63
		246,251		**120,178**

The Group is exposed to foreign exchange risk in respect of cash and cash equivalents which are held in a currency other than the entity’s functional currency. The Group is also exposed to foreign exchange risk in respect of its subsidiary as its functional currency is euro. Accordingly, future changes in exchange rates will expose the Group to currency gains or losses that will impact the reported amounts of assets, liabilities, income and expenses and the impact could be material.

For the year ended December 31, 2025, the Group recognized a foreign exchange gain of $1.8 million (2024: gain of $2.1 million, 2023: loss of $2.6 million). The foreign exchange gain primarily relates to the Group's foreign currency holdings of cash, cash equivalents and other financial assets and the associated strengthening and weakening of those foreign currencies throughout the year. In the year ended December 31, 2024, the foreign exchange gain primarily related to the U.S. dollar cash and other financial assets holding of its subsidiary and the associated strengthening of the U.S. dollar. At December 31, 2025, if foreign currency exchange rates had strengthened/weakened by 10% against the U.S. dollar, with all other variables held constant, the loss before tax for the year would have been $8.0 million higher/lower (2024: $2.3 million higher/lower).

The Group does not believe there is currently a need to enter into specific contracts to reduce the exposure to changes in foreign exchange rates, such as by entering into options or forward contracts. The Group may in the future consider using options or forward contracts to manage currency transaction exposures. All marketable securities are denominated in U.S. dollar and are not subject to foreign exchange risk as they are held in an entity whose functional currency is the U.S. dollar. Other financial assets are denominated in U.S. dollar but are held in an entity whose functional currency is not the U.S. dollar and as such are subject to foreign exchange risk.

Credit risk

The Group is exposed to credit risk on our cash, cash equivalents and marketable securities. The Group's cash balance is maintained with well-established, highly rated financial institutions. As of December 31, 2025, the cash balance is held at three banks that have a minimum S&P's credit rating of A-. At December 31, 2025, the amount reflected in the statement of financial position for cash and cash equivalents represents the Group's maximum exposure to credit risk for these instruments.

At December 31, 2025, the Group holds investments in investment grade bonds and in money market funds ("the Portfolio"). These investments are exposed to credit risk in the event of default of the counterparty. The Group does not invest in equity instruments or derivatives and none of the bonds are individually above 3% of the value of the Portfolio.

The Group's marketable securities, measured at FVOCI, are subject to the expected credit loss model. The Group provides for expected credit losses as prescribed by IFRS 9 for its assets held at FVOCI. The expected credit loss model under IFRS 9 requires the calculation of "12 month expected credit losses" for financial assets. Those are the losses based on defaults which are possible within 12 months of the reporting date. This is required unless the asset is not considered to be of low credit risk at the reporting date and is deemed to have had a significant increase in credit risk since initial recognition. If that is the case, lifetime expected credit losses should be recorded. Management considers low credit risk for existing marketable securities to be an investment grade credit rating with at least one major rating agency. Assets held at FVOCI are considered to have low credit risk when they have a low risk of default and the issuer has a strong capacity to meet its contractual cash flow obligations in the short term. The Group's current policy is to invest primarily in investment grade securities. After a downgrade, compliance with this restriction is restored in a timely manner. The credit risk for the Group's marketable securities is considered to be low as of December 31, 2025. The impairment allowance recognized during the period was calculated based on 12 month expected credit losses and reconciles to the opening impairment allowance as follows:

	Year ended December 31,	
	2025 $'000	**2024 $'000**
Opening impairment allowance	**54**	**120**
Movement in impairment allowance during the year	(42)	(66)
Closing impairment allowance	**12**	**54**

The impairment allowance is based on assumptions around probability of default, loss given default, exposure at default and the discount rate. Judgment is used in making these assumptions and selecting the inputs to the expected credit losses calculation, based on any historical experience and current market conditions, as well as forward looking estimates at the end of the reporting period.

Interest rate risk

Interest rate risk is the risk of a change in the price of a financial instrument due to fluctuations in interest rates, leading to a financial loss. The Group is exposed to interest rate risk on its marketable securities. Although the bonds pay interest at a fixed rate, the value of the Group's marketable securities would decrease in the short term in the event of an interest rate increase in alternative investments.

As of December 31, 2025, if interest rates had increased / decreased by 50 basis points, with all other variables held constant, the Group's total comprehensive loss would have been $0.1 million higher / lower (2024: $0.3 million higher / lower), due to the movement in the fair value of the Group's marketable securities.

Liquidity risk

Liquidity risk is the risk that the Group may not be able to generate sufficient cash resources to settle its obligations in full as they fall due or can do so only on terms that are materially disadvantageous. Prudent liquidity risk management implies maintaining sufficient cash to cover working capital requirements. Cash is monitored by the Group's management.

Funding and liquidity risks are reviewed regularly by the Board of Directors and management. The Group funds its capital requirements through capital raising. All financial liabilities, aside from lease liabilities as included in Note 15 "Leases", are due within one year from the balance sheet date.

Capital management

The Group considers capital as equivalent to the IFRS equity on the balance sheet (including share capital, additional paid-in capital and all other equity reserves attributable to the owners of the Company). The Group has no interest-bearing debt.

The Group's objectives when managing capital are to safeguard the Group's ability to continue as a going concern and to provide returns to its shareholders through advancing our investigational pharmaceutical product candidates towards regulatory approval.

Fair value estimation

The carrying amount is considered to be a reasonable approximation of fair value for the following financial assets and liabilities:

- Cash
- Other current assets; and
- Trade payables and other current liabilities.

The following table shows the carrying amounts and fair values of financial assets. The table does not include fair value information for financial assets or financial liabilities not measured at fair value if the carrying amount is a reasonable approximation of fair value.

	Carrying amount			
	2025	2025	2024	2024
	FVOCI $'000	FVTPL $'000	FVOCI $'000	FVTPL $'000
Financial assets measured at fair value				
Marketable securities	34,457	—	62,446	—
Cash equivalents	—	215,279	—	72,214
Other financial assets	—	—	—	19,387
	34,457	**215,279**	**62,446**	**91,601**

Fair value methodology

The Group uses the following hierarchy for determining and disclosing the fair value of financial instruments:

Level 1: Quoted prices (unadjusted) in active markets for identical assets and liabilities.

Level 2: Inputs other than quoted market prices within Level 1 that are observable for the asset, either directly or indirectly.

Level 3: If one or more of the significant inputs is not based on observable market data, the instrument is included in level 3. This is the case for unlisted equity securities.

The fair value of marketable securities, other financial assets and cash equivalents are based on quoted market prices representing Level 1 inputs.

Fair value – share-based compensation

Fair values must be estimated on an ongoing basis with regard to awards under the Share Option Plan. The approach to valuation follows the grant date fair value principle and the key input factors are described for the share-based compensation awards in Note 18, "Share-based compensation".

20. Related party disclosures

There have been no transactions with related parties, other than share options granted to members of key management, in the year ended December 31, 2025, that had a material effect on the financial position or performance of the Group (2024: none). For further information, see Note 18 "Share-based compensation".

Key Management Compensation

Key management are those persons who have the authority and responsibility for planning, directing and controlling the activities of the Group. Key management is comprised of executive officers and the Board of Directors who served during the reporting period.

	Year ended December 31,		
	2025 $'000	**2024 $'000**	**2023 $'000**
Salary and related expenses	1,622	1,870	1,421
Pension contributions	85	61	-
Share-based compensation expense	7,444	1,227	590
Other compensation	-	260	-
	9,151	**3,418**	**2,011**

21. Loss per share

The basic loss per share is calculated by dividing the loss for the year attributable to shareholders by the weighted average number of shares in issue during the financial year as follows:

	Year ended December 31,		
	2025	**2024**	**2023**
Loss attributable to shareholders (in $'000)	(48,258)	(38,961)	(35,587)
Weighted average number of shares in issue	61,042,621	52,028,145	52,022,588
Basic and diluted loss per share (in USD)	(0.79)	(0.75)	(0.68)

For the years ended December 31, 2025, 2024 and 2023, basic and diluted loss per share are calculated on the weighted average number of shares issued and outstanding and exclude shares to be issued under the Share Option Plan, as the effect of including those shares would be anti-dilutive.

22. Events after the reporting date

There were no events after the reporting date requiring disclosure in the Group's consolidated financial statements.

Exhibit 2.1

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following description of our share capital is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to Irish law, including without limitation the Irish Companies Act 2014 (as amended) (referred to herein as the Irish Companies Act), and by reference to our Constitution, a copy of which is incorporated by reference as an exhibit to the Annual Report on Form 20-F of which this exhibit is a part. We encourage you to review applicable Irish law and our Constitution for additional information.

The Company

We are a public limited company incorporated under the laws of Ireland. We were incorporated on March 29, 2021, to become a holding company for GH Research Ireland Limited. GH Research Ireland Limited was originally incorporated under the laws of Ireland on October 16, 2018, as GH Research Limited. GH Research Limited changed its name to GH Research Ireland Limited on March 29, 2021. Pursuant to the terms of the Corporate Reorganization (as defined below), all shareholders of GH Research Ireland Limited exchanged each of the shares held by them for shares in GH Research PLC of the same share classes with the same shareholder rights and, as a result, GH Research Ireland Limited became a wholly-owned subsidiary of GH Research PLC.

We are registered with the Companies Registration Office in Ireland under company registration number 691405 and our principal place of business is at Joshua Dawson House, Dawson Street, Dublin 2, D02 RY95, Ireland.

Our objects, detailed in Clause 3 of our memorandum of association, found in our Constitution, are varied and wide ranging and include, among other things, the carrying on of the business of a holding company and of the businesses of a researcher, developer, manufacturer, distributor, wholesaler, retailer, service provider, investor, trader and any other business which may seem to our Board of Directors capable of being conveniently carried on in connection with these objects or calculated directly or indirectly to enhance the value of or render more profitable any of our property. For a more fulsome description of our objects, we encourage you to review the full version of our Constitution, a copy of which is incorporated by reference as an exhibit to the Annual Report on Form 20-F of which this exhibit is a part.

For further information on our Constitution, please see "—Key Provisions of our Constitution" below.

Authorized and Issued Share Capital

Pursuant to the terms of a share for share exchange agreement dated May 27, 2021, all shareholders of GH Research Ireland Limited exchanged each of the shares held by them for ordinary shares of GH Research PLC of the same share classes with the same shareholder rights as the shares held by them in GH Research Ireland Limited and, as a result, GH Research Ireland Limited became a wholly-owned subsidiary of GH Research PLC (referred to herein as the Corporate Reorganization).

Pursuant to a shareholder resolution of GH Research PLC dated June 24, 2021, we effected (a) the conversion of (i) 5,923,079 Series A preferred shares of nominal value $0.01 each into 5,923,079 ordinary shares of nominal value $0.01 each and (ii) 25,379,047 Series B preferred shares of nominal value $0.01 each into 25,379,047 ordinary shares of nominal value $0.01 each and (b) the 2.50-for-one share consolidation of the ordinary shares of nominal value $0.01 each into ordinary shares of nominal value $0.025 each, such that the authorized share capital of the Company was thereafter $1,000,000,000 divided into 40,000,000,000 ordinary shares of nominal value $0.025 (collectively referred to herein as the Share Consolidation), immediately after the SEC declared the registration statement for our initial public offering effective.

As of December 31, 2025, the issued and outstanding share capital of GH Research PLC was 62,029,395 ordinary shares of nominal value $0.025 per share.

Ordinary Shares

Our ordinary shares have a nominal value of $0.025 per share. Further details of the rights attaching to the ordinary shares are set out in the comparison table below and in the Constitution. In accordance with the Constitution, the following summarizes the rights of our ordinary shares:

- The holders of ordinary shares are entitled to one vote for each ordinary share held of record on all matters submitted to a vote of the shareholders;
- The holders of our ordinary shares shall be entitled to receive notice of, attend, speak and vote at our general meetings and receive a copy of every report, accounts, circular or other documents sent out by us to our shareholders; and
- The holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders or in the case of an interim dividend, declared by our directors.

Stock Exchange Listing

Our ordinary shares are listed on the Nasdaq Global Market, under the symbol "GHRS".

Transfer Agent and Registrar of Shares

Our share register is kept by Computershare Trust Company, N.A., which acts as transfer agent and registrar. The share register reflects only record owners of our shares. Irish law does not recognize fractional shares held of record.

Key Provisions of our Constitution

The Constitution was adopted on June 24, 2021 and a summary of certain key provisions of the Constitution is set out below. The summary below is not a complete copy of the terms of the Constitution. For further information, please refer to the full version of the Constitution, a copy of which is incorporated by reference as an exhibit to this Annual Report on Form 20-F of which this exhibit is a part.

The Constitution contains, among other things, provisions to the following effect:

Share Capital

The share capital consists of ordinary shares, nominal value $0.025 per share. Our authorized share capital consists of $1,000,000,000 divided into 40,000,000,000 ordinary shares, nominal value $0.025 per share.

We may issue shares subject to the maximum authorized share capital contained in our Constitution. The authorized share capital may be increased or reduced by a simple majority of the votes of the shareholders cast at a general meeting (which is referred to under Irish law as an ordinary resolution). The shares comprising our authorized share capital may be divided into shares of such nominal value as such resolution shall prescribe. As a matter of Irish company law, the directors of a company may issue new ordinary shares without shareholder approval once authorized to do so by the Constitution or by an ordinary resolution adopted by the shareholders at a general meeting. The authorization may be granted for a maximum period of five years, so it must be renewed by the shareholders by an ordinary resolution on or before the expiry of this term (if we wish to issue shares). At our annual general meeting of shareholders in 2025, our shareholders authorized our Board of Directors to allot new ordinary shares up to the amount of our authorized share capital without shareholder approval for a period of five years, which will expire on July 30, 2030.

The rights and restrictions to which the ordinary shares are subject are prescribed in the Constitution.

The holders of our ordinary shares are entitled to one vote for each ordinary share upon all matters presented to our shareholders. Subject to any preferences granted to other classes of our securities that may be outstanding in the future (including any preferred shares that may be created), there are no voting right restrictions or preferences with respect to our shareholders.

Irish law does not recognize fractional shares held of record. Accordingly, the Constitution does not provide for the issuance of fractional shares of ours, and our register of members, or the register of members, does not reflect any fractional shares.

Whenever an alteration or reorganization of the share capital of ours would result in any of our shareholders becoming entitled to fractions of a share, our Board of Directors may, on behalf of those shareholders that would become entitled to fractions of a share, arrange for the sale of the shares representing fractions and the distribution of the net proceeds of sale in due proportion among the shareholders who would have been entitled to the fractions.

Voting

All matters, other than those requiring a special resolution, may be approved by a simple majority of the members present (in person or by proxy) at any general meeting. The presence, in person or by proxy, of one or more persons holding or representing by proxy at least 25% of the votes that may be cast by all members constitutes a quorum for the conduct of business.

At any of our meetings, all resolutions put to our shareholders will be decided on a poll.

Irish company law requires certain matters to be approved by not less than 75% of the votes cast at a general meeting of our shareholders (which is referred to under Irish law as a special resolution). Examples of matters requiring special resolutions include:

- amending the Constitution;
- approving a change of name of GH Research PLC;
- authorizing the entering into of a guarantee or provision of security in connection with a loan, quasi-loan or credit transaction to a director or connected person;
- opting out of preemption rights on the issuance of new shares for cash;
- our re-registration from a public limited company to a private company;
- variation of class rights attaching to classes of shares (where the Constitution does not provide otherwise);
- purchase of our shares off-market;
- reduction of issued share capital;
- sanctioning a compromise/scheme of arrangement;
- resolving that we be wound up by the Irish courts;
- resolving in favor of a shareholders' voluntary winding up;
- re-designation of shares into different share classes; and
- setting the reissue price of treasury shares.

Variation of Rights

Where our shares are divided into different classes, the rights attaching to a class of shares may only be varied or abrogated if (a) the holders of 75% in nominal value of the issued shares of that class consent in writing to the variation, or (b) a special resolution, passed at a separate general meeting of the holders of that class, sanctions the variation. The quorum at any such separate general meeting, other than an adjourned meeting, shall be one person holding or representing by proxy a majority in nominal value of the issued shares of the class in question and the quorum at an adjourned meeting shall be one person holding or representing by proxy shares of the class in question or that person's proxy. The rights conferred upon the holders of any class of shares issued with preferred or other rights shall not, unless otherwise expressly provided by the terms of issue of the shares of that class, be deemed to be varied by a purchase or redemption by us of our own shares or by the creation or issue of further shares ranking pari passu therewith or subordinate thereto.

Dividends

Under Irish law, dividends and distributions may only be made from distributable profits. Distributable profits, broadly, means the accumulated realized profits of a company, less accumulated realized losses of the company on a standalone basis. In addition, no dividend or distribution may be made unless the net assets of the company are not less than the aggregate of the company's called up share capital plus undistributable reserves and the distribution does not reduce the company's net assets below such aggregate. Undistributable reserves include a company's undenominated capital (effectively its share premium and capital redemption reserve) and the amount by which the company's accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed the company's accumulated unrealized losses, so far as not previously written off in a reduction or reorganization of capital. The determination as to whether or not the company has sufficient distributable profits to fund a dividend must be made by reference to "relevant financial statements" of the company. The "relevant financial statements" are either the last set of unconsolidated annual audited financial statements or unaudited financial statements prepared in accordance with the Irish Companies Act, which give a "true and fair view" of the company's unaudited unconsolidated financial position in accordance with accepted accounting practice in Ireland. These "relevant financial statements" must be filed in the Companies Registration Office (the official public registry for companies in Ireland).

The Constitution authorizes the Board to declare such interim dividends as appear justified from the profits of the company without the approval of the shareholders. The dividends can be declared and paid in the form of cash or non-cash assets, subject to applicable law. We may pay dividends in any currency. The Board may deduct from any dividend or other moneys payable to any shareholder all sums of money, if any, due from the shareholder to the company in respect of our ordinary shares.

We may, by ordinary resolution, declare final dividends to be paid to our shareholders. However, no dividend shall exceed the amount recommended by the Board of Directors. The Board of Directors may also pay to the shareholders such dividends as interim or final dividends as appear to the directors to be justified by our profits.

We have never declared or paid any cash dividend, and do not anticipate declaring or paying any cash dividends in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. See "Item 3. Key Information D. Risk Factors — Risks Related to the Ownership of Our Ordinary Shares." Because there is no present intention to pay dividends on our ordinary shares for the foreseeable future, capital appreciation, if any, will be a shareholder's sole source of gains and such shareholder may never receive a return on the shareholder's investment.

For information about the Irish tax considerations relating to dividend payments, see "Item 10. Additional Information —E. Taxation."

Liquidation

Our duration will be unlimited. We may be dissolved and wound up at any time by way of a shareholders' voluntary winding up or a creditors' winding up. In the case of a shareholders' voluntary winding up, a special resolution of the shareholders is required. We may also be dissolved by way of court order on the application of a creditor, or by the Companies Registration Office as an enforcement measure in circumstances where we fail to file certain returns.

The rights of the shareholders to a return of our assets on dissolution or winding up, following the settlement of all claims of creditors, are prescribed in the Constitution and may be further prescribed in the terms of any preferred shares we create and issue from time to time. In particular, if we have created and issued any preferred shares, holders of such preferred shares may have the right to priority in our dissolution or winding up. The Constitution provides that, subject to the priorities of any creditors, the assets will be distributed to the shareholders in proportion to the paid up nominal value of the shares held by such shareholder. The Constitution provides that the shareholders are entitled to participate pro rata in a winding up, but their right to do so is subject to the rights of any holders of the shares issued upon special terms and conditions to participate under the terms of any series or class of such shares.

Preemption Rights

Under Irish law, certain statutory preemption rights apply automatically in favor of shareholders where shares are to be issued for cash. However, as permitted by Irish law, we have opted out of these preemption rights by way of special resolution passed at our 2025 annual general meeting of shareholders. Irish law requires that this opt-out is renewed at least every five years by a special resolution of our shareholders. As a result, our shareholders must renew this opt-out authorization no later than July 30, 2030. If the opt-out is not renewed, as a general rule, shares issued for cash must be offered to our existing shareholders on a pro rata basis to their existing shareholding before any of our shares may be issued to any new shareholders. Statutory preemption rights do not apply (i) where shares are issued wholly or partly for non-cash consideration (such as in a stock-for-stock acquisition), (ii) to the issue of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any income or capital distribution) or (iii) where shares are issued pursuant to an employee option or similar equity plan.

Alteration of Share Capital

Under our Constitution, we may, by ordinary resolution, divide any or all of our share capital into shares of a smaller nominal value than our existing shares (often referred to as a share split) or consolidate any or all of our share capital into shares of larger nominal value than our existing shares (often referred to as a reverse share split).

We may, by ordinary resolution, reduce the authorized but unissued share capital. We may, by special resolution and subject to confirmation by the Irish High Court, reduce the issued share capital and any undenominated share capital.

Board of Directors

Appointment of Directors

The Constitution provides for a minimum of two directors and a maximum of nine directors. Our shareholders may from time to time increase or reduce the maximum number, or increase the minimum number, of directors by ordinary resolution. Our Board of Directors determines the number of directors within the range of two to nine. Our Constitution does not require directors to retire on account of age.

Proceedings of Directors

Subject to the provisions of our Constitution, our Board of Directors may regulate their proceedings as they deem appropriate. A director may, and the secretary at the request of a director shall, call a meeting of the directors. The quorum for a meeting of our Board of Directors shall be fixed from time to time by decision of the Board of Directors, but it must never be fewer than two directors (or duly appointed alternate directors). Questions and matters requiring resolution arising at a meeting shall be decided by a majority of votes of the participating directors, with each director having one vote. In the case of an equality of votes, the chairperson will have a second or casting vote (unless the chairperson is not entitled to vote on the resolution in question).

Conflicts of Interest

Our directors have certain statutory and fiduciary duties as a matter of Irish law. All of the directors have equal and overall responsibility for management of our Company (although directors who also serve as employees may have additional responsibilities and duties arising under their employment agreements (if applicable), and it is likely that more will be expected of them in compliance with their duties than non-executive directors). The Irish Companies Act provides specifically for certain fiduciary duties of the directors of Irish companies, including duties:

- to act in good faith and in the best interests of the company;
- to act honestly and responsibly in relation to the company's affairs;
- to act in accordance with the company's constitution and to exercise powers only for lawful purposes;
- not to misuse the company's property, information and/or opportunity;

- not to fetter their independent judgment;
- to avoid conflicts of interest;
- to exercise care, skill and diligence; and
- to have regard for the interests of the company's shareholders.

Other statutory duties of directors include ensuring the maintenance of proper books of account, having annual accounts prepared, having an annual audit performed, maintaining certain registers, making certain filings and disclosing personal interests. Directors of public limited companies such as ourselves will have a specific duty to ensure that the company secretary is a person with the requisite knowledge and experience to discharge the role. Directors may rely on information, opinions, reports or statements, including financial statements and other financial data, prepared or presented by (1) other directors, officers or employees of the company whom the director reasonably believes to be reliable and competent in the matters prepared or presented, (2) legal counsel, public accountants or other persons as to matters the director reasonably believes to be within their professional or expert competence or (3) a committee of the board of which the director does not serve as to matters within its designated authority, which committee the director reasonably believes to merit confidence.

Our Constitution provides that a director shall generally not vote at a meeting of the directors or a committee of directors on any resolution concerning a matter in which he or she has, directly or indirectly or together with any person or persons connected with him or her an interest which is material or a duty which conflicts or may conflict with the interests of the Company.

Directors' and Officers' Indemnity

To the fullest extent permitted by Irish law, the Constitution contains indemnification for the benefit of, amongst others, our directors, company secretary and executive officers. However, as to our directors and company secretary, this indemnity is limited by the Irish Companies Act, which prescribes that an advance commitment to indemnify only permits a company to pay the costs or discharge the liability of a director or company secretary where judgment is given in favor of the director or company secretary in any civil or criminal action in respect of such costs or liability, or where an Irish court grants relief because the director or company secretary acted honestly and reasonably and ought fairly to be excused. Any provision whereby an Irish company seeks to commit in advance to indemnify its directors or company secretary over and above the limitations imposed by the Irish Companies Act will be void, whether contained in the company's constitution or any contract between the company and the director or company secretary. This restriction does not apply to our executive officers who are not directors, or other persons who would not be considered "officers" within the meaning of the Irish Companies Act.

Our Constitution also contains indemnification and expense advancement provisions for persons who are not directors or our corporate secretary.

We are permitted under the Constitution and the Irish Companies Act to take out directors' and officers' liability insurance, as well as other types of insurance, for our directors, officers, employees and agents. In order to attract and retain qualified directors and officers, we maintain customary directors' and officers' liability insurance and other types of comparable insurance.

General Meetings

We are required to hold an annual general meeting in each calendar year within nine months of our fiscal year-end and with no more than 15 months elapsing between annual general meetings.

Notice of an annual general meeting must be given to all of our shareholders and to our auditors. The Constitution provides for a minimum notice period for an annual general meeting of 21 clear days, which is the minimum permitted under Irish law.

Generally speaking, the only matters which must, as a matter of Irish company law, be transacted at an annual general meeting are the presentation of the annual statutory financial statements, balance sheet and reports of the directors and auditors, the appointment of new auditors and the fixing of the auditor's remuneration (or delegation of same). If no resolution is made in respect of the reappointment of an existing auditor at an annual general meeting, the existing auditor will be deemed to have continued in office. Where the constitution of a company so provides, as our Constitution does, additional matters may be required to be transacted such as the election and re-election of directors.

As provided under Irish law, extraordinary general meetings may be convened (i) by our Board of Directors, (ii) by request of our shareholders holding not less than 10% of our paid up share capital carrying voting rights for so long as our shares are not admitted to trading on a regulated market in any member state of the EU, (iii) by request of our statutory auditor in connection with its resignation or (iv) in exceptional cases, by court order.

Notice of an extraordinary general meeting must be given to all our shareholders and to our auditors. Under Irish law and the Constitution, the minimum notice period of 21 clear days' prior written notice applies, except that in the case of an extraordinary general meeting, if the company offers facilities to members to vote by electronic means and shareholders have passed a special resolution at the immediately preceding general meeting approving such shortened notice period, an extraordinary general meeting can be called with 14 clear days' prior written notice (provided that no special resolutions are proposed to be put to a vote at that meeting). The notice periods prescribed for the convening of general meetings are on the basis of "clear" days, meaning the deemed date of receipt of the notice and the date of the meeting itself are not counted towards the minimum number of days' notice required.

In the case of an extraordinary general meeting convened by our shareholders, the proposed purpose of the meeting must be set out in the requisition notice. Upon receipt of any such valid requisition notice, the Board of Directors has 21 days to convene a meeting of our shareholders to vote on the matters set out in the requisition notice. This meeting must be held within two months of the receipt of the requisition notice. If the Board of Directors does not convene the meeting within such 21-day period, the requisitioning shareholders, or any of them representing more than one half of the total voting rights of all of them, may themselves convene a meeting, which meeting must be held within three months of our receipt of the requisition notice.

If the Board of Directors becomes aware that our net assets are not greater than half of the amount of our called up share capital, the directors must convene an extraordinary general meeting of shareholders not later than 28 days from the date that they learn of this fact to consider how to address the situation.

Borrowing Powers

Subject to the Constitution and the Irish Companies Act, our Board of Directors may exercise all of our powers to:

(i) borrow money;

(ii) indemnify and guarantee;

(iii) mortgage or charge;

(iv) create and issue debentures and other securities; and

(v) give security either outright or as collateral security for any of our debt, liability or obligation or any of a third party.

Uncertificated Shares

Shares in an Irish public limited company such as ours can, in principle, be issued and held either in a so-called certificated (i.e., hard copy share certificates are issued to shareholders) or a so-called uncertificated (i.e., dematerialized) form. All shareholders' names must be entered into the register of members maintained by an Irish public limited company in order to acquire legal title to the shares.

To make shares in an Irish public limited company deliverable for trading on an exchange, the shares are required to be issued in uncertificated form.

Amendment of Constitution

Irish company law requires a special resolution of our shareholders (approval by not less than 75% of the votes cast at a general meeting of our shareholders) to approve any amendments to the Constitution.

Anti-Takeover Provisions of Irish Law

Irish Takeover Rules and Substantial Acquisition Rules

A transaction in which a third party seeks to acquire 30% or more of our voting rights and any other acquisitions of our securities will be governed by the Irish Takeover Panel Act 1997 and the Irish Takeover Rules made thereunder, the Irish Takeover Panel Act, 1997, Takeover Rules, 2022, or the Irish Takeover Rules, and will be regulated by the Irish Takeover Panel. The general principles of the Irish Takeover Rules, or the General Principles, and certain important aspects of the Irish Takeover Rules are described below.

General Principles

The Irish Takeover Rules are built on the following General Principles which will apply to any transaction regulated by the Irish Takeover Panel:

(i) in the event of an offer, all holders of securities of the target company must be afforded equivalent treatment and, if a person acquires control of a company, the other holders of securities must be protected;

(ii) the holders of securities in the target company must have sufficient time and information to enable them to reach a properly informed decision on the offer; where it advises the holders of securities, the board of directors of the target company must give its views on the effects of the implementation of the offer on employment, employment conditions and the locations of the target company's place of business;

(iii) a target company's board of directors must act in the interests of that company as a whole and must not deny the holders of securities the opportunity to decide on the merits of the offer;

(iv) false markets must not be created in the securities of the target company, the bidder or any other company concerned by the offer in such a way that the rise or fall of the prices of the securities becomes artificial and the normal functioning of the markets is distorted;

(v) a bidder can only announce an offer after ensuring that he or she can fulfill in full the consideration offered, if such is offered, and after taking all reasonable measures to secure the implementation of any other type of consideration;

(vi) a target company may not be hindered in the conduct of its affairs longer than is reasonable by an offer for its securities; and

(vii) a "substantial acquisition" of securities, whether such acquisition is to be effected by one transaction or a series of transactions, shall take place only at an acceptable speed and shall be subject to adequate and timely disclosure.

Transfer of Shares

Under certain circumstances, a person who acquires shares, or other voting securities, of a company may be required under the Irish Takeover Rules to make a mandatory cash offer for the remaining outstanding voting securities in that company at a price not less than the highest price paid for the securities by the acquiror, or any parties acting in concert with the acquiror, during the previous 12 months. This mandatory bid requirement is triggered if an acquisition of securities would increase the aggregate holding of an acquiror, including the holdings of any parties acting in concert with the acquiror, to securities representing 30% or more of the voting rights in a company, unless the Irish Takeover Panel otherwise consents. An acquisition of securities by a person holding, together with its concert parties, securities representing between 30% and 50% of the voting rights in a company would also trigger the mandatory bid requirement if, after giving effect to the acquisition, the percentage of the voting rights held by that person, together with its concert parties, would increase by 0.05% within a 12-month period. Any person, excluding any parties acting in concert with the holder, holding securities representing more than 50% of the voting rights of a company is not subject to these mandatory offer requirements in purchasing additional securities.

Voluntary Bid; Requirements to Make a Cash Offer and Minimum Price Requirement

If a person makes a voluntary offer to acquire our outstanding ordinary shares, the offer price must not be less than the highest price paid for our ordinary shares by the bidder or its concert parties during the three-month period prior to the commencement of the offer period. The Irish Takeover Panel has the power to extend the "look back" period to 12 months if the Irish Takeover Panel, taking into account the General Principles, believes it is appropriate to do so.

If the bidder or any of its concert parties has acquired our ordinary shares (1) during the 12-month period prior to the commencement of the offer period that represent more than 10% of our total ordinary shares or (2) at any time after the commencement of the offer period, the offer must be in cash or accompanied by a full cash alternative and the price per share must not be less than the highest price paid by the bidder or its concert parties during, in the case of clause (1), the 12-month period prior to the commencement of the offer period or, in the case of (2), the offer period. The Irish Takeover Panel may apply this Rule to a bidder who, together with its concert parties, has acquired less than 10% of our total ordinary shares in the 12-month period prior to the commencement of the offer period if the Irish Takeover Panel, taking into account the General Principles, considers it just and proper to do so.

An offer period will generally commence from the date of the first announcement of the offer or proposed offer.

Substantial Acquisition Rules

The Irish Takeover Rules also contain rules governing substantial acquisitions of shares and other voting securities which restrict the speed at which a person may increase his or her holding of shares and rights over shares to an aggregate of between 15% and 30% of the voting rights of the company. Except in certain circumstances, an acquisition or series of acquisitions of shares or rights over shares representing 10% or more of the voting rights of the company is prohibited, if such acquisition(s), when aggregated with shares or rights already held, would result in the acquirer holding 15% or more but less than 30% of the voting rights of the company and such acquisitions are made within a period of seven days. These rules also require accelerated disclosure of acquisitions of shares or rights over shares relating to such holdings.

Takeover Timeline

Under the Irish Takeover Rules, in certain circumstances a strict 42-day deadline will be imposed within which a person with whom we are in talks, or from whom we have received an approach, regarding a possible offer is required to make a firm offer for the Company, or announce they will not be making an offer. The Irish Takeover Panel may agree to extend this deadline at our request. This deadline may deter potential bidders from making an offer for the Company.

Frustrating Action

Under the Irish Takeover Rules, our Board of Directors is not permitted to take any action that might frustrate an offer for our shares once our Board of Directors has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (1) the issue of shares, options, restricted share units or convertible securities, (2) the redemption or repurchase of securities by the company (save in certain circumstances), (3) material acquisitions or disposals, (4) entering into contracts other than in the ordinary course of business or (5) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our Board of Directors has reason to believe an offer is or may be imminent. Exceptions to this prohibition are available where:

(a) the action is approved by our shareholders at a general meeting; or

(b) the Irish Takeover Panel has given its consent, where:

(i) it is satisfied the action would not constitute frustrating action;

(ii) our shareholders holding more than 50% of the voting rights state in writing that they approve the proposed action and would vote in favor of it at a general meeting;

(iii) the action is taken in accordance with a contract entered into prior to the announcement of the offer, or any earlier time at which our Board of Directors considered the offer to be imminent; or

(iv) the decision to take such action was made before the announcement of the offer and either has been at least partially implemented or is in the ordinary course of business.

Shareholders' Rights Plan

Irish law does not expressly authorize or prohibit companies from issuing share purchase rights or adopting a shareholder rights plan as an anti-takeover measure. However, there is no directly relevant case law on the validity of such plans under Irish law. In addition, such a plan would be subject to the Irish Takeover Rules and the General Principles underlying the Irish Takeover Rules. The Constitution allows our Board of Directors to adopt a shareholder rights plan upon such terms and conditions as our Board of Directors deems expedient and in the best interests of us, subject to applicable law.

Subject to the Irish Takeover Rules, our Board of Directors also has power to issue any of our authorized and unissued shares on such terms and conditions as it may determine and any such action should be taken in our best interests. It is possible, however, that the terms and conditions of any issue of preference shares could discourage a takeover or other transaction that holders of some or a majority of the ordinary shares believe to be in their best interests or in which holders might receive a premium for their shares over the then-market price of the shares.

Disclosure of Interests in Shares

Under the Irish Companies Act, our shareholders must notify us if, as a result of a transaction, the shareholder will become interested in 3% or more of our voting shares, or if as a result of a transaction a shareholder who was interested in 3% or more of our voting shares ceases to be so interested. Where a shareholder is interested in 3% or more of our voting shares, the shareholder must notify us of any alteration of his or her interest that brings his or her total holding through the nearest whole percentage number, whether an increase or a reduction. The relevant percentage figure is calculated by reference to the aggregate nominal value of the voting shares in which the shareholder is interested as a proportion of the entire nominal value of our issued share capital (or any such class of share capital in issue). Where the percentage level of the shareholder's interest does not amount to a whole percentage, this figure may be rounded down to the next whole number. We must be notified within five business days of the transaction or alteration of the shareholder's interests that gave rise to the notification requirement. If a shareholder fails to comply with these notification requirements, the shareholder's rights in respect of any of our shares it holds will not be enforceable, either directly or indirectly. However, such person may apply to the court to have the rights attaching to such shares reinstated.

In addition to these disclosure requirements, we, under the Irish Companies Act, may, by notice in writing, require a person whom we know or have reasonable cause to believe to be, or at any time during the three years immediately preceding the date on which such notice is issued to have been, interested in shares comprised in our relevant share capital to (i) indicate whether or not it is the case and (ii) where such person holds or has during that time held an interest in our shares, provide additional information, including the person's own past or present interests in our shares. If the recipient of the notice fails to respond within the reasonable time period specified in the notice, we may apply to the Irish court for an order directing that the affected shares be subject to certain restrictions, as prescribed by the Irish Companies Act, as follows:

(i) any transfer of those shares or, in the case of unissued shares, any transfer of the right to be issued with shares and any issue of shares, shall be void;

(ii) no voting rights shall be exercisable in respect of those shares;

(iii) no further shares shall be issued in right of those shares or in pursuance of any offer made to the holder of those shares; and

(iv) no payment shall be made of any sums due from us on those shares, whether in respect of capital or otherwise.

The court may also order that shares subject to any of these restrictions be sold with the restrictions terminating upon the completion of the sale.

In the event we are in an offer period pursuant to the Irish Takeover Rules, accelerated disclosure provisions apply for persons holding an interest in our securities of 1% or more.

Comparison of Irish Law and Delaware Law

As a public limited company incorporated under the laws of Ireland, the rights of our shareholders are governed by applicable Irish law, including the Irish Companies Act, and not by the law of any U.S. state. As a result, our directors and shareholders are subject to different responsibilities, rights and privileges than are applicable to directors and shareholders of U.S. corporations. The applicable provisions of the Irish Companies Act differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Irish Companies Act applicable to us and the General Corporation Law of the State of Delaware relating to shareholders' rights and protections. The applicable provisions in respect of the Company under the Constitution is also set out where relevant. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and Irish law. You are also urged to carefully read the relevant provisions of the Delaware General Corporation Law and the Irish Companies Act for a more complete understanding of the differences between Delaware and Irish law.

	IRELAND	DELAWARE
Number of Directors	The Irish Companies Act provides for a minimum of two directors. The Constitution provides for a minimum of two directors and a maximum of nine. Our shareholders may from time to time increase or reduce the maximum number, or increase the minimum number, of directors by ordinary resolution. Our Board of Directors determines the number of directors within the range of two to nine.	A typical certificate of incorporation and bylaws would provide that the number of directors on the board of directors will be fixed from time to time by a vote of the majority of the authorized directors. Under Delaware law, a board of directors can be divided into classes and cumulative voting in the election of directors is only permitted if expressly authorized in a corporation's certificate of incorporation.
Removal of Directors	Under the Irish Companies Act, the shareholders may, by ordinary resolution, remove a director from office before the expiration of his or her term, at a meeting held with no less than 28 days' notice and at which the director is entitled to be heard. Because of this provision of the Irish Companies Act, a director may be so removed before the expiration of his or her period of office The power of removal is without prejudice to any claim for damages for breach of contract (e.g., employment contract) that the director may have against the Company in respect of his or her removal. The Constitution also provides that the office of a director will also be vacated if the director is restricted or disqualified to act as a director under the Irish Companies Act; resigns his or her office by notice in writing to us or in writing offers to resign and the directors resolve to accept such offer; or is requested to resign in writing by not less than 75% of the other directors.	A typical certificate of incorporation and bylaws provide that, subject to the rights of holders of any preferred shares, directors may be removed at any time by the affirmative vote of the holders of at least a majority, or in some instances a supermajority, of the voting power of all of the then outstanding shares entitled to vote generally in the election of directors, voting together as a single class. A certificate of incorporation could also provide that such a right is only exercisable when a director is being removed for cause (removal of a director only for cause is the default rule in the case of a classified board).

	IRELAND	DELAWARE
Vacancies on the Board of Directors	Any vacancy on our Board of Directors, including a vacancy resulting from an increase in the number of directors or from the death, resignation, retirement, disqualification or removal of a director, shall be deemed a casual vacancy. Any casual vacancy shall only be filled by the decision of a majority of our Board of Directors then in office, provided that a quorum is present and provided that the appointment does not cause the number of directors to exceed any number fixed by or in accordance with the Constitution as the maximum number of directors. Any director elected to fill a vacancy resulting from an increase in the number of directors shall hold office for the remaining term of office. Any director elected to fill a vacancy not resulting from an increase in the number of directors shall have the same remaining term as that of his predecessor. A director retiring at a meeting shall retain office until the close or adjournment of the meeting.	A typical certificate of incorporation and bylaws provide that, subject to the rights of the holders of any preferred shares, any vacancy, whether arising through death, resignation, retirement, disqualification, removal, an increase in the be filled by a majority vote of the remaining directors, even if such directors remaining in office constitute less than a quorum, or by the sole remaining director. Any newly elected director usually holds office for the remainder of the full term expiring at the annual meeting of shareholders at which the term of the class of directors to which the newly elected director has been elected expires.

	IRELAND	DELAWARE
Annual General Meeting	We are required to hold annual general meetings at intervals of no more than 15 months after the previous annual general meeting, provided that an annual general meeting is held in each calendar year following our first annual general meeting, no more than nine months after our fiscal year-end. The only matters which must, as a matter of Irish company law, be transacted at an annual general meeting are the consideration of the Irish statutory financial statements, the report of the directors, the report of the auditors on those statements and that report and a review by the members of our affairs. If no resolution is made in respect of the reappointment of an auditor at an annual general meeting, the previous auditor will be deemed to have continued in office.	Typical bylaws provide that annual meetings of shareholders are to be held on a date and at a time fixed by the board of directors.
General Meeting	Our extraordinary general meetings may be convened by (i) our Board of Directors, (ii) on requisition of shareholders holding not less than 10% of our paid up share capital carrying voting rights or (iii) on requisition of our auditors. Extraordinary general meetings are generally held for the purposes of approving shareholder resolutions as may be required from time to time. If our directors become aware that our net assets are half or less of the amount of our called up share capital, our directors must convene an extraordinary general meeting of our shareholders not later than 28 days from the date that they learn of this fact. This meeting must be convened for the purposes of considering whether any, and if so what, measures should be taken to address the situation.	Under Delaware law, a special meeting of shareholders may be called by the board of directors or by any other person authorized to do so in the certificate of incorporation or the bylaws.

	IRELAND	DELAWARE
Notice of General Meetings	Notice of a general meeting must be given to all our shareholders and to our auditors. The minimum notice periods are 21 clear days' notice in writing for an annual general meeting or an extraordinary general meeting to approve a special resolution and 14 clear days' notice in writing for any other extraordinary general meeting (if the company offers facilities to members to vote by electronic means and shareholders have passed a special resolution at the immediately preceding general meeting approving such shortened notice period). General meetings may be called by shorter notice, but only with the consent of our auditors and all of our shareholders entitled to attend and vote thereat. Because of the 21-clear day and 14-clear day requirements described in this paragraph, the Constitution includes provisions reflecting these requirements of Irish law. In the case of an extraordinary general meeting convened by our shareholders, the proposed purpose of the meeting must be set out in the requisition notice. Upon receipt of this requisition notice, our Board of Directors has 21 days to convene a meeting of our shareholders to vote on the matters set out in the requisition notice. This meeting must be held within two months of the receipt of the requisition notice. If our Board of Directors does not convene the meeting within such 21-day period, the requisitioning shareholders, or any of them representing more than one-half of the total voting rights of all of them, may themselves convene a meeting, which meeting must be held within three months of the receipt of the requisition notice.	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than 10 nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.

	IRELAND	DELAWARE
Quorum	The presence, in person or by proxy, of one or more persons holding or representing by proxy at least 25% of the votes that may be cast at the relevant time constitutes a quorum for the conduct of business at a general meeting. No business may take place at a general meeting if a quorum is not present in person or by proxy. Our Board of Directors has no authority to waive quorum requirements stipulated in the Constitution. Abstentions and broker non-votes will be counted as present for purposes of determining whether there is a quorum in respect of the proposals.	Under Delaware law, a corporation's certificate of incorporation or bylaws can specify the number of shares which constitute the quorum required to conduct business at a meeting, provided that in no event shall a quorum consist of less than one-third of the shares entitled to vote at a meeting.
Proxy	Under Irish law, a shareholder may designate another person to attend, speak and vote at a general meeting of the company on their behalf by proxy, which proxy need not be a shareholder. Where interests in shares are held by a nominee trust company, this company may exercise the rights of the beneficial holders on their behalf as their proxy. Voting rights may be exercised by shareholders registered in the share register as of the record date for the meeting or by a duly appointed proxy of such a registered shareholder, which proxy need not be a shareholder. Where interests in shares are held by a nominee trust company, this company may exercise the rights of the beneficial holders on their behalf as their proxy. All proxies must be appointed in accordance with the Constitution. The Constitution permits the appointment of proxies by our shareholders to be notified to us electronically, when permitted by our directors.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

	IRELAND	DELAWARE
Issue of New Shares	Under the Constitution, we may issue shares subject to the maximum authorized share capital contained in the Constitution. The authorized share capital may be increased or reduced by a resolution approved by a simple majority of the votes cast at a general meeting of our shareholders, referred to under Irish law as an "ordinary resolution." As a matter of Irish law, the directors of a company may issue new ordinary shares without shareholder approval once authorized to do so by its constitution or by an ordinary resolution adopted by its shareholders at a general meeting. The authorization may be granted for a maximum period of five years, at which point it may be renewed by shareholders by an ordinary resolution. At our annual general meeting of shareholders in 2025, our shareholders authorized our Board of Directors to issue new ordinary shares up to the amount of our authorized share capital without shareholder approval for a period of five years, which will expire on July 30, 2030.	Under Delaware law, if the company's certificate of incorporation so provides, the directors have the power to authorize the issuance of additional stock. The directors may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the company or any combination thereof.

	IRELAND	DELAWARE
Preemptive Rights	Under Irish law, unless otherwise authorized, when an Irish public limited company issues shares for cash to new shareholders, it is required first to offer those shares on the same or more favorable terms to existing shareholders of the company on a pro rata basis, commonly referred to as the statutory preemption right. However, as permitted by Irish law, we have opted out of these preemption rights by way of special resolution passed at our 2025 annual general meeting of shareholders. A special resolution requires not less than 75% of the votes cast at a general meeting of our shareholders. Irish law requires that this opt-out is renewed at least every five years by a special resolution of our shareholders. As a result, our shareholders must renew this opt-out authorization no later than July 30, 2030. If the opt-out is not renewed, shares issued for cash must be offered to our preexisting shareholders pro rata before the shares can be issued to any new shareholders. The statutory preemption rights do not apply where shares are issued for non-cash consideration and do not apply to the issue of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any income or capital distribution) or where shares are issued pursuant to an employee option or similar equity plan.	Under Delaware law, stockholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.

	IRELAND	DELAWARE
Authority to Allot	Under the Constitution, we may issue shares subject to the maximum authorized share capital contained in the Constitution. The authorized share capital may be increased or reduced by a resolution approved by a simple majority of the votes cast at a general meeting of our shareholders, referred to under Irish law as an "ordinary resolution." Our authorized share capital may be divided into shares of such nominal value as the resolution shall prescribe. As a matter of Irish law, the directors of a company may issue new ordinary shares without shareholder approval once authorized to do so by its constitution or by an ordinary resolution adopted by its shareholders at a general meeting. The authorization may be granted for a maximum period of five years, at which point it may be renewed by shareholders by an ordinary resolution. At our annual general meeting of shareholders in 2025, our shareholders authorized our Board of Directors to issue new ordinary shares up to the amount of our authorized share capital without shareholder approval for a period of five years, which will expire on July 30, 2030.	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. The board may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.

	IRELAND	DELAWARE
Acquisition of Own Shares	Under Irish law, a company may issue redeemable shares and redeem them out of distributable reserves or the proceeds of a new issue of shares for that purpose. All redeemable shares must also be fully paid. Redeemable shares may, upon redemption, be cancelled or held in treasury. The Constitution provides that shareholder approval will not be required to deem any shares redeemable. We may also be given an additional general authority by our shareholders to purchase our own shares on-market, which would take effect on the same terms and be subject to the same conditions as applicable to purchases by our subsidiaries as described below. Repurchased and redeemed shares may be cancelled or held as treasury shares. The nominal value of treasury shares that we hold at any time must not exceed 10% of the nominal value of our issued share capital. We may not exercise any voting rights in respect of any shares held as treasury shares. We may either cancel or, subject to certain conditions, reissue treasury shares. Under Irish law, an Irish or non-Irish subsidiary may purchase our shares either on-market or off-market. For a subsidiary of ours to make on-market purchases of our shares, the shareholders must provide general authorization for such purchase by way of ordinary resolution. However, as long as this general authority has been granted, no specific shareholder authority for a particular on-market purchase by a subsidiary of our shares is required. For an off-market purchase by a subsidiary of ours, the proposed purchase contract must be authorized by special resolution of our shareholders before the contract is entered into. This authority must specify the date on which the authority is to expire, which shall not be more than 18 months from the date the special resolution was passed. The person whose shares of ours are to be bought cannot vote in favor of the special resolution and, for at least 21 days prior to the special resolution being passed, the purchase contract must be on display or must be available for inspection by our shareholders at our registered office.	Under Delaware law, any corporation may purchase or redeem its own shares, except that generally it may not purchase or redeem these shares if the capital of the corporation is impaired at the time or would become impaired as a result of the redemption. A corporation may, however, purchase or redeem out of capital shares that are entitled upon any distribution of its assets to a preference over another class or series of its shares if the shares are to be retired and the capital reduced.

	IRELAND	DELAWARE
Different Classes of Shares	Without prejudice to any rights attached to any existing shares, we may issue shares with such rights or restrictions as we determine by an ordinary resolution approved by our shareholders. As a matter of Irish company law, the directors of a company may issue new ordinary shares without shareholder approval once authorized to do so by the constitution or by an ordinary resolution adopted by the shareholders at a general meeting. The authorization may be granted for a maximum period of five years, at which point it must be renewed by the shareholders by an ordinary resolution (if we wish to issue shares). The Constitution authorizes our Board of Directors to issue new ordinary shares without shareholder approval for a period of five years from the date of adoption of our Constitution. We may also issue shares which are, or are liable to be, redeemed at the option of us or the holder. Whenever our share capital is divided into different classes of shares, the special rights attached to any class may be varied or abrogated either with the written consent of the holders of 75% in nominal value of the issued shares of the class (excluding shares held as treasury shares) or with the sanction of a special resolution passed at a separate meeting of the holders of the shares of the class (but not otherwise), and may be so varied or abrogated either while we are a going concern or during or in contemplation of a winding up. The rights conferred upon the holders of any class of shares issued with preferred or other rights shall not, unless otherwise expressly provided by the terms of issue of the shares of that class, be deemed to be varied by our purchase or redemption of our own shares or by the creation or issue of further shares ranking pari passu therewith or subordinate thereto.	A company's Delaware's certificate of incorporation may authorize the board of directors: (1) to provide for the issuance of one or more series of preferred stock; (2) to establish from time to time the number of shares to be included in such series; and (3) to fix the designations, preferences and relative, participating, optional or other special rights, and qualifications, limitations or restrictions of each such series.

	IRELAND	DELAWARE
Dividends	Under Irish law, dividends and distributions may only be made from distributable reserves which are, generally, a company's accumulated realized profits less its accumulated realized losses. In addition, no distribution or dividend may be made if our net assets are not, or if making such distribution or dividend will cause our net assets to not be, equal to, or in excess of, the aggregate of our called up share capital plus undistributable reserves. Undistributable reserves include the company's undenominated capital and the amount by which a company's accumulated unrealized profits exceeds its accumulated unrealized losses. The determination as to whether or not we have sufficient distributable reserves to fund a dividend must be made by reference to our most recent unconsolidated annual audited financial statements or other financial statements properly prepared in accordance with the Irish Companies Act. The relevant financial statements must be filed in the Companies Registration Office (the official public registry for companies in Ireland). The Constitution authorizes our Board of Directors to declare an interim dividend without shareholder approval to the extent they appear justified by profits of the Company available for distribution. Our Board of Directors may also recommend a dividend to be approved and declared by the shareholders at a general meeting, provided that no dividend issued may exceed the amount recommended by the directors.	Under Delaware law, subject to any restriction in the corporation's certificate of incorporation, the Board may declare and pay dividends out of: (1) surplus of the corporation, which is defined as net assets less statutory capital; or (2) if no surplus exists, out of the net profits of the corporation for the year in which the dividend is declared and/or the preceding year; provided, however, that if the capital of the corporation has been diminished to an amount less than the aggregate amount of capital represented by the issued and outstanding stock of all classes having preference upon the distribution of assets, the Board may not declare and pay dividends out of the corporation's net profits until the deficiency in the capital has been repaired.

	IRELAND	DELAWARE
General Provisions Governing a Liquidation; Liquidation Distributions	Our duration will be unlimited. We may be dissolved and wound up at any time by way of a shareholders' voluntary winding up or a creditors' winding up. In the case of a shareholders' voluntary winding up, a special resolution of our shareholders is required. We may also be dissolved by way of court order on the application of a creditor, or by the Companies Registration Office as an enforcement measure where we have failed to file certain returns. The rights of the shareholders to a return of our assets on dissolution or winding up, following the settlement of all claims of creditors, are prescribed in the Constitution.	Upon the dissolution of a Delaware corporation, after satisfaction of the claims of creditors, the assets of that corporation would be distributed to stockholders in accordance with their respective interests, including any rights a holder of shares of preference shares may have to preferred distributions upon dissolution or liquidation of the corporation.
Amendment of Constitution	Irish company law requires a special resolution of our shareholders (approval by not less than 75% of the votes cast at a general meeting of our shareholders) to approve any amendments to the Constitution.	***Amendment of Certification of Incorporation and Bylaws*** Under Delaware law, amendments to a corporation's certificate of incorporation require the approval of stockholders holding a majority of the outstanding shares entitled to vote on the amendment. If a class vote on the amendment is required by the Delaware General Corporation Law, a majority of the outstanding stock of the class is required, unless a greater proportion is specified in the certificate of incorporation or by other provisions of the Delaware General Corporation Law. Under the Delaware General Corporation Law, the board of directors may amend bylaws if so authorized in the certificate of incorporation. The stockholders of a Delaware corporation also have the power to amend bylaws.

	IRELAND	DELAWARE
Reduction of Share Capital	We may reduce our authorized but unissued share capital in any manner permitted by the Irish Companies Act. We also may, by special resolution (approved by not less than 75% of the votes cast at a general meeting of our shareholders) and subject to confirmation by the Irish High Court, reduce our issued share capital in any way permitted by the Irish Companies Act. For purposes of Irish law, repurchases of our shares may be effected by a redemption if the repurchased shares are redeemable shares or are deemed to be redeemable shares by the Constitution. The Constitution provides that, unless the Board of Directors determines otherwise, each of our shares shall be deemed to be a redeemable share on, and from the time of, the existence or creation of an agreement, transaction or trade between us and any person pursuant to which we acquire or will acquire our shares, or an interest in our shares, from the relevant person. Redeemable shares of ours shall have the same characteristics as any other of our shares save that they shall be redeemable in accordance with the arrangement.	Under Delaware law, a corporation, by an affirmative vote of a majority of the board of directors, may reduce its capital by reducing or eliminating the capital represented by shares of capital stock which have been retired, by applying to an already authorized purchase redemption, conversion or exchange of outstanding shares of its capital stock some or all of the capital represented by shares being purchased, redeemed, converted or exchanged or any capital that has not been allocated to any particular class of capital stock or by transferring to surplus capital some or all of the capital not represented by any particular class of its capital stock or the capital associated with certain issued shares of its par value capital stock. No reduction of capital may be made unless the assets of the corporation remaining after the reduction are sufficient to pay any debts for which payment has not otherwise been provided.

	IRELAND	DELAWARE
Rights of Inspection	Under Irish law, our shareholders have the right to: (i) receive a copy of the Constitution; (ii) inspect and obtain copies of the minutes of our general meetings and resolutions; (iii) inspect and receive a copy of our register of members, register of directors and secretaries, register of directors' interests, register of directors' service contracts and memoranda and other statutory registers that we maintain; (iv) receive copies of balance sheets and directors' and auditors' reports that have previously been sent to our shareholders prior to an annual general meeting; and (v) receive balance sheets of any of our subsidiaries that have previously been sent to our shareholders prior to an annual general meeting for the preceding 10 years.	Delaware law allows any stockholder in person or by attorney or other agent, upon written demand under oath stating the purpose thereof, during the usual hours for business to inspect for any proper purpose, and to make copies and extracts from: (1) the corporation's stock ledger, a list of its stockholders, and its other books and records; and (2) a subsidiary's books and records, to the extent that: (a) the corporation has actual possession and control of such records of such subsidiary; or (b) the corporation could obtain such records through the exercise of control over such subsidiary, provided that as of the date of the making of the demand: (i) the stockholder inspection of such books and records of the subsidiary would not constitute a breach of an agreement between the corporation or the subsidiary and a person or persons not affiliated with the corporation; and (ii) the subsidiary would not have the right under the law applicable to it to deny the corporation access to such books and records upon demand by the corporation.

	IRELAND	DELAWARE
Liability of Directors and Officers	To the fullest extent permitted by Irish law, the Constitution contains indemnification for the benefit of, among others, our directors, company secretary and executive officers. However, as to our directors and company secretary, this indemnity is limited by the Irish Companies Act, which prescribes that an advance commitment to indemnify only permits a company to pay the costs or discharge the liability of a director or company secretary where judgment is given in favor of the director or company secretary in any civil or criminal action in respect of such costs or liability, or where an Irish court grants relief because the director or company secretary acted honestly and reasonably and ought fairly to be excused. Any provision whereby an Irish company seeks to commit in advance to indemnify its directors or company secretary over and above the limitations imposed by the Irish Companies Act will be void, whether contained in its Constitution or any contract between the company and the director or company secretary. This restriction does not apply to our executive officers who are not directors, our company secretary or other persons who would be considered "officers" within the meaning of the Irish Companies Act. The Constitution also contains indemnification and expense advancement provisions for persons who are not directors or our corporate secretary. We are permitted under the Constitution and the Irish Companies Act to take out directors' and officers' liability insurance, as well as other types of insurance, for our directors, officers, employees and agents. In order to attract and retain qualified directors and officers, we maintain customary directors' and officers' liability insurance and other types of comparable insurance.	Delaware law permits a corporation's certificate of incorporation to include a provision eliminating or limiting the personal liability of a director or officer (but not other controlling persons) of the corporation for monetary damages for breach of a fiduciary duty as a director or officer. However, no provision can eliminate or limit the liability of: (1) a director or officer for any breach of his or her duty of loyalty to the corporation or its stockholders; (2) a director or officer for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law; (3) a director for intentional or negligent payment of unlawful dividends or stock purchases or redemptions; (4) a director or officer for any transaction from which he or she derives an improper personal benefit; or (5) an officer in any action by or in right of the corporation.

	IRELAND	DELAWARE
Voting Rights	Under the Constitution, each holder of our ordinary shares is entitled to one vote for each ordinary share that he or she holds as of the record date for the meeting. We may not exercise any voting rights in respect of any shares held as treasury shares. Any shares held by our subsidiaries will count as treasury shares for this purpose, and such subsidiaries cannot therefore exercise any voting rights in respect of those shares.	Each stockholder is entitled to one vote for each share of capital stock held by the stockholder, unless the certificate of incorporation provides otherwise. If issued, the voting rights of holders of preferred stock will be determined by the certificate of incorporation or the certificate of designation with respect to such preferred stock.
Shareholder Vote on Certain Transactions	Pursuant to Irish law, shareholder approval in connection with a transaction involving the Company would be required under the following circumstances: • in connection with a scheme of arrangement, both a court order from the Irish High Court and the approval of a majority in number representing 75% in value of the shareholders present and voting in person or by proxy at a meeting called to approve such a scheme would be required; • in connection with a conversion of the Company by way of cross-border conversion under the EU (Cross-Border Conversions, Mergers and Divisions) Regulations 2023 (referred to herein as the Irish Mobility Regulations), approval by a special resolution of the shareholders would be required; • in connection with an acquisition of the Company by way of a merger with an EU company under the Irish Mobility Regulations, approval by a special resolution of the shareholders would be required; and • in connection with a merger with an Irish company under the Irish Companies Act, approval by a special resolution of shareholders would be required.	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: • the approval of the board of directors; and • the approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of the corporation entitled to vote on the matter.

	IRELAND	DELAWARE
Standard of Conduct for Directors	The directors of the Company have certain statutory and fiduciary duties as a matter of Irish law. All of the directors have equal and overall responsibility for the management of the Company (although directors who also serve as employees may have additional responsibilities and duties arising under their employment agreements (if applicable), and it is likely that more will be expected of them in compliance with their duties than non-executive directors). The Irish Companies Act provides specifically for certain fiduciary duties of the directors of Irish companies, including duties: • to act in good faith and in the best interests of the company; • to act honestly and responsibly in relation to the company's affairs; • to act in accordance with the company's constitution and to exercise powers only for lawful purposes; • not to misuse the company's property, information and/or opportunity; • not to fetter their independent judgment; • to avoid conflicts of interest; • to exercise care, skill and diligence; and • to have regard for the interests of the company's shareholders. Other statutory duties of directors include ensuring the maintenance of proper books of account, having annual accounts prepared, having an annual audit performed, maintaining certain registers, making certain filings and disclosing personal interests. Directors of public limited companies such as the Company will have a specific duty to ensure that the company secretary is a person with the requisite knowledge and experience to discharge the role. Directors may rely on information, opinions, reports or statements, including financial statements and other financial data, prepared or presented by (1) other directors, officers or employees of the company whom the director reasonably believes to be reliable and competent in the matters prepared or presented, (2) legal counsel, public accountants or other persons as to matters the director reasonably believes to be within their professional or expert competence or (3) a committee of the board of which the director does not serve as to matters within its designated authority, which committee the director reasonably believed to merit confidence.	Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interests of the stockholders. Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself or herself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or breakup of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the stockholders.

	IRELAND	DELAWARE
Shareholder Suits	In Ireland, the decision to institute proceedings is generally taken by a company's board of directors, who will usually be empowered to manage the company's business. In certain limited circumstances, a shareholder may be entitled to bring a derivative action on behalf of the company. The central question at issue in deciding whether a minority shareholder may be permitted to bring a derivative action is whether, unless the action is brought, a wrong committed against the company would otherwise go unredressed. The principal case law in Ireland indicates that to bring a derivative action a person must first establish a prima facie case (i) that the company is entitled to the relief claimed and (ii) that the action falls within one of the five exceptions derived from case law, as follows: (1) where an ultra vires or illegal act is perpetrated; (2) where more than a bare majority is required to ratify the "wrong" complained of; (3) where the shareholders' personal rights are infringed; (4) where a fraud has been perpetrated upon a minority by those in control; or	Under Delaware law, a stockholder may bring a derivative action on behalf of the corporation to enforce the rights of the corporation. An individual also may commence a class action suit on behalf of himself or herself and other similarly situated stockholders where the requirements for maintaining a class action under the Delaware General Corporation Law have been met. A person may institute and maintain such a suit only if such person was a stockholder at the time of the transaction which is the subject of the suit or his or her shares thereafter devolved upon him or her by operation of law. Additionally, under Delaware case law, the plaintiff generally must be a stockholder not only at the time of the transaction which is the subject of the suit, but also through the duration of the derivative suit. The Delaware General Corporation Law also requires that the derivative plaintiff make a demand on the directors of the corporation to assert the corporate claim before the suit may be prosecuted by the derivative plaintiff, unless such demand would be futile.

IRELAND	DELAWARE
(5) where the justice of the case requires a minority to be permitted to institute proceedings. Shareholders may also bring proceedings against the company where the affairs of the company are being conducted, or the powers of the directors are being exercised, in a manner oppressive to the shareholders or in disregard of their interests. Oppression connotes conduct that is burdensome, harsh or wrong. Conduct must relate to the internal management of the company. This is an Irish statutory remedy and the court can grant any order it sees fit, usually providing for the purchase or transfer of the shares of any shareholder.	

Exhibit 4.1

Rules

of the

GH Research PLC Share Option Plan

Board Approval on June 20, 2021 (and amended on May 15, 2025)

Contents

GH Research PLC

Share Option Plan

1 Establishment and Purpose

The Plan was adopted by a resolution of the Board of Directors of the Company passed on June 20, 2021. The purpose of the Plan is to attract, retain, and motivate employees and directors of GH Research plc, its subsidiaries and affiliates, to provide for competitive compensation opportunities, to encourage long term service, to recognize individual contributions and reward achievement of performance goals, and to promote the creation of long term value for shareholders by aligning the interests of such persons with those of shareholders.

2 Definitions

2.1 In the Plan, the following expressions bear the following meanings and all references to statutes are to Irish statutes:

the **Act** means the Taxes Consolidation Act 1997;

Acquiring Company means a company that obtains Control of the Company in accordance with Rule 14;

Adoption Date means the date on which the Board adopts this Plan;

Board means the board of directors for the time being of the Company or the directors present at a duly convened meeting of the board of directors of the Company at which a quorum is present or a duly constituted committee of such board;

Control means control as defined in Section 11 of the Act;

Committee means the remuneration committee of the Board or such other committee constituted by the Board for the purpose of administering the Plan;

Company means GH Research plc registered in Ireland under registration number 691405;

Date of Grant means the date on which the Grantor grants an Option to an Eligible Person, which date will be borne on the Option Agreement communicating the grant of an Option hereunder as provided in Rule 6.6;

Director means a director of the Company or any other member of the Group who is not an active employee of the Company or any other company that is a member of the Group;

Eligible Person means any person who is a Director or employee of a member of the Group;

Exercise Price means the price payable by the Participant to acquire Shares subject to an Option, subject to any adjustment under Rule 16;

Grantor means the Company;

Group means the Company and its Subsidiaries (and references to Group Company or member of the Group will be construed accordingly);

Health Reasons means reasons of ill health which as certified by a medical practitioner (approved by the Committee) compel a Participant to discontinue or alter the nature of his employment, office or occupation;

Market Value means the market price of a Share, determined in accordance with Rule 5.3;

Option means an award of a right under Rule 6 entitling the holder to purchase or subscribe for Shares;

Option Agreement means any written agreement, contract, or other instrument or document setting out details of an Option in the form prescribed by Rule 6.6;

Participant means any Eligible Person who is for the time being the holder of part or all of an Option granted under the Plan;

Performance Conditions means the conditions attached to an Option as prescribed in an Option Agreement;

Performance Period means the period in respect of which any Performance Condition is to be satisfied as set out in an Option Agreement;

Plan means the Company's Share Option Plan consisting of these plan rules together with any sub-plans, as amended from time to time in accordance with the provisions in that regard herein contained;

Share means an ordinary share of US$0.025 each in the capital for the time being of the Company;

Stock Exchange means any recognised stock exchange on which Shares are traded (including NASDAQ or any successor body) and, if more than one, such stock exchange as the Committee determines;

Subsidiary means any company which is, for the time being, a subsidiary of the Company within the meaning of Section 7 of the Companies Act, 2014;

Termination of Service means, unless otherwise defined in an applicable Option Agreement, that a Participant is no longer employed by, nor a director of, the Company or any other member of the Group, as the case may be. A Participant employed by a Subsidiary of the Company will also be deemed to incur a Termination of Service if the Subsidiary of the Company ceases to be such a Subsidiary, and the Participant does not immediately thereafter become an employee of the Company or another Subsidiary of the Company. Temporary absences from employment or service because of illness, vacation or leave of absence and transfers among the Company and its Subsidiaries will not be considered a Termination of Service.

2.2 Where the context permits the singular will include the plural and vice versa and the masculine will include the feminine. Headings are to be ignored in construing the terms of the Plan.

2.3 References to any statute will include any statutory modification, amendment or re-enactment thereof.

3 Administration

The Plan will be administered by the Committee, and the Committee will have full and final authority to exercise discretion and make any determinations under the Plan, subject to and consistent with the provisions of the Plan. Any action of the Committee with respect to the Plan will be final, conclusive, and binding on all persons, including the Company, Subsidiaries, Eligible Persons, any person claiming any rights under the Plan from or through any Eligible Person, and shareholders. By accepting an Option under the Plan, each Eligible Person accepts the authority and discretion of the Committee as set forth in, and exercised in accordance with, this Plan. The express grant of any specific power to the Committee, and the taking of any action by the Committee, will not be construed as limiting any power or authority of the Committee. The Committee may delegate to other members of the Board or officers or managers of the Company or any Subsidiary the authority, subject to such terms as the Committee will determine, to perform administrative functions and to perform such other functions as the Committee may determine, to the extent permitted by applicable law.

4 Eligibility for participation

4.1 The Plan is available for Eligible Persons who will be nominated for that purpose by the Committee.

4.2 The Committee will at its absolute discretion determine whether or not a person is an Eligible Person and will nominate such persons for participation in the Plan.

4.3 No person will be entitled as of right to participate in the Plan and the decision as to who will have the opportunity of participating and the time and extent of his participation will, subject to the terms of the Plan, be made by the Committee in its absolute discretion.

5 Limitation as to Participation

5.1 No Option will be capable of being granted under the Plan more than ten years after the Adoption Date.

5.2 If at the relevant time:

5.2.1 the Company’s shares are listed on a Stock Exchange, the Market Value of a Share will be determined by the Committee by reference to the closing price of a Share on the dealing day immediately preceding the Date of Grant or, if the Committee so determines, by reference to an averaging of closing prices over a period of up to 5 dealing days immediately preceding the Date of Grant.

5.2.2 If the Company's shares are not listed on a Stock Exchange, the Market Value of a Share will be determined by the Company in accordance with section 548 of the Act.

5.2.3 For the avoidance of doubt an Option which has lapsed due to failure to meet applicable Performance Conditions set out in the relevant Option Agreement within the Performance Period (or similar criteria under any other share incentive plan adopted by the Company or its Subsidiaries) or otherwise will not be taken into account for the purpose of this Rule 5.

6 Grant of Options

6.1 The Grantor may at any time within ten years from the Adoption Date grant Options to one or more Participants.

6.2 Any Options granted under the Plan must be approved in advance by the Committee, which will have absolute discretion in respect of the approval of Options.

6.3 The Committee may determine that a nominal amount of consideration will be payable by a Participant in respect of the grant of an Option.

6.4 Each Option granted will be evidenced by an Option Agreement given to the Participant. Option Agreements may be in writing or in such other form as the Grantor determines and the Committee approves.

6.5 Each Option Agreement will specify:

6.5.1 the Date of Grant of the Option;

6.5.2 the number of Shares subject to the Option;

6.5.3 the Exercise Price;

6.5.4 the Performance Conditions and Performance Period, if any, to be satisfied as a condition of the vesting of the Option in accordance with the Option Agreement; and

6.5.5 such additional terms and conditions of the Option as the Committee may from time to time prescribe, including, but not limited to, conditions relating to transferability or forfeiture, exercisability and waiver or accelerations thereof, and waivers of performance conditions relating to an Option, based in each case on such considerations as the Committee will determine.

6.6 When issuing Option Agreements the Grantor will:

6.6.1 refer the Participant to all the provisions of the Plan; and

6.6.2 notify the Participant of his right to renounce the Option under Rule 6.8.

6.7 A Participant to whom an Option has been granted may by notice in writing given to the Grantor within 30 days from the Date of Grant renounce his rights thereunder and in such case the Option will be deemed never to have been granted.

6.8 An Option which has been granted to a Participant will be treated as having been accepted unless a renunciation in writing in respect thereof has been received by the Grantor from such person under Rule 6.8.

6.9 In the event that a Participant loses or misplaces his Option Agreement the Grantor may issue a replacement in writing or in such other form as the Grantor determines, upon application in writing by the Participant.

7 Limitations on Grant of Options

7.1 Unless otherwise resolved by the Committee, the number of Shares for which Options may be granted under the Plan on any day will not, when added to the number of Shares which immediately prior to that day will have been or remain to be issued or purchased on the market pursuant to Options granted during the period of ten years immediately preceding that day under the Plan or any other share incentive plan adopted by the Company or its Subsidiaries, exceed options over 3,721,251 of the number of Shares for the time being in issue.

7.2 Calculating limits

For the avoidance of doubt:

7.2.1 Shares which will have been the subject of Options or rights which have lapsed will not be taken into account for the purposes of this Rule 7.

7.2.2 Shares acquired by a trustee of any employee's trust established by the Company in conjunction with this Plan, or acquired by any third party in conjunction with this Plan, which have been counted as issued or purchased on the market for the purposes of this Rule 7 will not also be counted when they are delivered to Participants to satisfy any Option.

8 Specific Terms of Options

8.1 Options may be granted on the terms and conditions set forth in this Rule 8. In addition, the Committee may impose on any Option or the vesting or exercise thereof, at the Date of Grant or thereafter (subject to Rule 6) such additional terms and conditions, not inconsistent with the provisions of the Plan, as the Committee will determine, including terms regarding forfeiture of Options or continued exercisability of Options in the event of Termination of Service of the Participant.

8.2 The Committee is authorised to grant Options to Eligible Persons on the following terms and conditions:

8.2.1 **Exercise Price**: Unless the Committee determines otherwise at the Date of Grant, the Exercise Price per Share in relation to an Option will be not less than the Market Value of a Share on the day preceding the Date of Grant, PROVIDED THAT in all cases it will not be less than the nominal value of a Share.

8.2.2 **Option Term**: The term of each Option will be determined by the Committee; provided, however, that such term will not be longer than eight years from the Date of Grant of the Option.

8.2.3 **Time and Method of Exercise**: The Committee will determine at the Date of Grant or thereafter the time or times at which an Option may be exercised in whole or in part (including, without limitation, upon achievement of performance criteria if deemed appropriate by the Committee), the methods by which such Exercise Price may be paid or deemed to be paid (including, without limitation, broker-assisted exercise arrangements), the form of such payment (cash or Shares), and the methods by which Shares will be delivered or deemed to be delivered to Eligible Persons.

9 Non-transfer of Option

Subject to Rule 10.2, the Options will be personal to a Participant and the Participant will not assign, transfer, sell, mortgage, charge, pledge or encumber in any way whatsoever the Option or any of the Shares subject to the Option or any interest therein. An Option will lapse forthwith if the Participant purports to assign, transfer it etc. as aforesaid.

10 Termination of Service

10.1 General Rule

Except where the provisions of Rule 10.2 or Rule 10.3 or a Participant's Option Agreement apply to provide otherwise in relation to the whole or a specified part of the Option, on a Termination of Service:

10.1.1 any part of the Option that has not vested as at the date of cessation will lapse immediately on that date; and

10.1.2 any part of the Option that has vested as at the date of cessation will lapse in full 30 days after the date of cessation to the extent not exercised by such date.

10.2 Death of Participant

Except as otherwise provided in a Participant's Option Agreement, if a Participant dies the Committee may determine that either the whole or a specified percentage of any Option held by such Participant at the date of his death will be capable of vesting in, being exercised by or otherwise transferred to his legal personal representative on such terms and conditions as they may determine. Unless the Committee determines that an Option will be transferred to the legal personal representative of a Participant, the Option will lapse automatically on the death of the Participant.

10.3 Good Leaver

10.4 In the event of a Termination of Service on account of:

10.4.1 Health Reasons;

10.4.2 with respect to Participants who are employees only, redundancy (within the meaning of the Redundancy Payments Acts 1967 to 2014);

10.4.3 any form of voluntary severance by agreement with the Company;

10.4.4 the transfer of the undertaking or part-undertaking in which the Participant is employed to a person other than a member of the Group;

10.4.5 the company by which the Participant is employed ceasing to be under the Control of the Group; or

10.4.6 any other reasons in the absolute discretion of the Committee where exceptional circumstances have arisen,

the Committee may in its absolute discretion determine the extent to which the Performance Conditions attaching to the Option, if any, have been satisfied, having due regard to that part of the Performance Period to which the Performance Conditions set out in the relevant Option Agreement apply which has then expired, and the Committee will specify what proportionate part, if any, of the Shares under the Option will vest. If no determination is made by the Committee under this Rule 10.4 the Option will lapse.

11 Clawback

If at any time in the 12 month period after the Date of Grant of an Option,

11.1 the Company is required to restate its accounts to a material extent; or

11.2 the Committee becomes aware of any material wrongdoing on the part of the Participant that would have entitled the Company to terminate the Participant's employment in accordance with the Participant's contract of employment

then (notwithstanding that such Participant's employment may not have been, or may not be, cancelled as a result of the wrongdoing in question) the Committee will be entitled to recalculate (in good faith) the number of Shares subject to the Option to reflect the number of Shares that it would have granted to the Participant under the Option had these facts been known at the time the Option was granted.

12 Procedure on Exercise of Options

12.1 Unless otherwise provided in the Option Agreement, an Option will be exercised by a Participant as follows:

12.1.1 The Participant will give notice in writing to the Company (in such form as the Committee may require from time to time) setting out the number of Shares over which the Participant wishes to exercise the Option and delivering such further details as the Committee may require to the Company. No exercise will be permitted without (i) the prior consent of the Committee and (ii) unless the Committee is satisfied at the relevant time that the Option is exercisable and (if then applicable) that such exercise would not breach any applicable laws or regulations, including but not limited to any code regarding the regulation of dealings in shares in the Company by employees or directors.

12.1.2 The Participant will make payment to the Company of the Exercise Price and any taxation in accordance with clause 15 as is applicable, at the same time as notification of exercise, by way of:

(a) delivery to the Company of cash in lawful currency or a bankers' draft in favour of the Company for the appropriate amount;

(b) delivery to the Company (on a form prescribed by the Committee) of an irrevocable direction approved by the Committee to sell the Shares and to deliver all or part of the sales proceeds to the Company in payment of all or such portion of the Exercise Price and, if directed any Taxation as is applicable; or

(c) payment by such other means as is consistent with applicable laws and regulations and agreed between the Company and the Participant.

12.2 Subject to the Company receiving any regulatory or other consent which is necessary to enable it to allot the Shares pursuant to the exercise of the Option and subject to the terms of any such consent, as soon as practicable after the notice exercising the Option has been received by the Company, the Committee on behalf of the Company will allot to the Participant the Shares in respect of which the notice has taken effect.

12.3 Shares allotted and issued in satisfaction of the exercise of the Option will rank pari passu in all respects with the other shares of the same class in issue at the date of the allotment, except for any restriction or any rights determined by reference to a date before the date of allotment and will be subject to all relevant provisions of the constitution of the Company and the provisions of the Companies Act 2014.

12.4 Shares transferred in satisfaction of the exercise of the Option will be transferred free of any lien, charge or other security interest, and with all rights attaching to them, other than any restriction or rights determined by reference to a date before the date of transfer.

12.5 If the Shares are listed or traded on a Stock Exchange, the Company will apply to the appropriate body for any newly issued Shares allotted on exercise of the Option to be listed or admitted to trading on that exchange. For the avoidance of doubt, all certificates for Shares and/or other securities delivered under the Plan pursuant to the exercise of Options shall be subject to such stop transfer orders and other restrictions as the Committee may deem advisable under the Plan or the rules, regulations and other requirements of the Securities and Exchange Commission, any Stock Exchange upon which such Shares or other securities are then listed or traded, and any applicable securities laws, and the Committee may cause a legend or legends to be put on any such certificates to make appropriate reference to such restrictions.

13 Lapse of Options

13.1 An Option will lapse and be forfeited on the occurrence of the earliest of the following:

13.1.1 the day following last day of the Option term, being the eighth anniversary of the Date of Grant (or such other date as determined by the Committee in accordance with Rule 8.2.2); or

13.1.2 the expiry of the Performance Period without the Performance Conditions having been satisfied or the date on which it becomes apparent that any such condition has become incapable of being satisfied; or

13.1.3 subject to Rule 10, the date on which a Termination of Service occurs; or

13.1.4 the date on which a resolution is passed for the winding up of the Company, or an order is made by any court for the compulsory winding-up of the Company; or

13.1.5 the date on which the Participant becomes bankrupt or does or attempts or omits to do anything as a result of which he is deprived of the beneficial ownership of the Shares.

13.2 Where a Participant is temporarily absent from his normal occupation with a member of the Group due to illness, vacation or other unpaid leave of absence, provided he returns to his normal occupation with a member of the Group within the agreed period an Option held by such Participant may be adjusted on a pro-rata basis in such proportion as the Committee may determine.

14 Change in Control of the Company, Reconstruction & Winding Up

14.1 Change in Control

Subject to Rule 14.2 and except as otherwise provided in a Participant’s Option Agreement, in the event that the Company or GH Research Ireland Limited is a party to a merger, sells all or substantially all of its assets, is subject to a takeover or other reorganisation including but not limited to a court-sanctioned compromise or arrangement, or the Committee considers this is about to occur, the Committee will be entitled (without the Participant's consent unless the Committee otherwise requires) at its discretion and notwithstanding anything herein contained (except the proviso below):

14.1.1 to accelerate vesting of Options in relation to the whole or a specified portion of the Shares to which such Options relate and within such time or times and subject to any other conditions or limitations as the Committee may at its discretion determine;

14.1.2 to agree that outstanding Options will be assumed or substituted by the surviving company or its parent (or the Acquiring Company or its parent where a takeover occurs) for Options which are equivalent to the Options originally granted under the Plan but which relate to shares in the surviving company or its parent (or the Acquiring Company or its parent where a takeover occurs);

14.1.3 to arrange for the continuation by the Company of outstanding Options (if the Company is a surviving company or an acquiring company in a takeover);

14.1.4 to make payment of a cash settlement to Participants equal, per Share, to the amount to be paid for one Share under the agreement of merger or takeover terms; or

14.1.5 to otherwise vary the outstanding Options on such conditions as the Committee may decide,

and the Committee may determine that any one or any combination of the above will occur. In the event that no such determination is made, or is not made in respect of a portion of an Option, the Option (or said portion of an Option) will lapse.

14.2 Re-organisation

Where the Company or GH Research Ireland Limited becomes a wholly-owned subsidiary of a holding company which will be owned in substantially the same proportions by the persons who held the Company's issued shares immediately before such transaction, the Committee may resolve with the agreement of the board of the holding company that Options granted hereunder will be treated as if they were in all respects options over shares in the holding company, but so that:

14.2.1 the new award will vest in the same manner as the Option;

14.2.2 the total market value of the new shares subject to the new award will, immediately after such reorganisation, be equal to the total market value of the Shares comprised in the Option immediately prior to such reorganisation;

14.2.3 the new award will be subject to performance conditions that will be at least equivalent (as determined by the Committee) to the Performance Conditions, if any, attaching to the Option;

14.2.4 the new shares will, at the date of any resolution by the Committee under this Rule 14.2, have the same rights attaching thereto as the Shares in the Company; and

14.2.5 the new award will be deemed to have been granted as at the Date of Grant of the Option.

14.3 Reconstruction and Winding-Up

In the event of:

14.3.1 any proposal for the reorganisation of the capital of the Company or for the reconstruction or amalgamation of the Company involving a material change in the nature of the Shares comprised in any Option (and for the purposes of this sub-rule the determination by the Committee of a material change in the nature of Shares in any particular case will be final and conclusive and will be communicated to each Participant in writing); or

14.3.2 the Company passing a resolution for its winding-up or an order being made for the compulsory winding-up of the Company (the passing of which resolution or the making of which order will be communicated by the Committee to each Participant in writing);

any Option held by a Participant may, at the discretion of the Committee, on the date that such proposal, reconstruction or amalgamation becomes unconditional or such winding-up takes effect or within such period before or after such date as the Committee may determine, vest on a pro-rata basis in such proportion as the Committee will determine and upon and subject to any conditions or limitations as the Committee may at its discretion determine. In the event that no such determination is made, or is not made in respect of a portion of an Option, the Option (or said portion of an Option) will lapse.

15 Tax Indemnity

15.1 The Participant will indemnify the Company (and, where relevant, any member of the Group) against any tax and social security contributions (or their equivalent in any jurisdiction) arising in respect of the Option which is a liability of the Participant but for which the Company or relevant member of the Group is required to account to a tax authority under the laws of any relevant territory. The Company may, to the extent permitted by law, recover the tax and social security from the Participant in such manner as the Committee think fit including (but without prejudice to the generality of the foregoing):

15.1.1 withholding Shares when the Option is exercised and selling same;

15.1.2 deducting the necessary amount from the Participant's remuneration; or

15.1.3 requiring the Participant to account directly to the Company or relevant tax authority for such tax and social security.

15.2 The Company will not be required to transfer any Shares to the Participant under the Plan until such obligations are satisfied.

16 Adjustments in the Event of Capitalisation and Rights Issues etc.

16.1 In the event of any alteration or re-organisation whatsoever taking place in the capital structure of the Company whether by way of capitalisation of profits or reserves, capital distribution, rights issue, consolidation or sub-division of Shares, the conversion of one class of share to another or reduction of capital or otherwise, the Committee may adjust any one or more of the following in such manner as is in the opinion of the Committee fair and reasonable:

16.1.1 the number of Shares subject to the Plan;

16.1.2 the definition of Share;

16.1.3 where the Option has been granted but no Shares have been delivered pursuant thereto, the number of Shares which may be delivered;

16.1.4 the Exercise Price per Share PROVIDED THAT this amount will not be reduced to less than the par value of a Share.

16.2 In the event of any alteration to the subject matter of an Option pursuant to the provisions of this Rule 16 the original Option Agreement will remain valid except to the extent modified by the alteration. The Grantor may issue revised Option Agreements or take whichever action it deems appropriate.

17 Alterations

17.1 Except to the extent prohibited by applicable law and unless otherwise expressly provided in a Option Agreement, the Committee may at any time and from time to time by resolution and without further formality alter, amend or revoke any provisions of the Plan in such manner as the Committee may consider necessary or desirable (including any retrospective, prospective or coincident alteration, amendment or revocation) PROVIDED THAT that no alteration, amendment or revocation shall be made without (i) shareholder approval, if such approval is required by applicable law or the rules of the Stock Exchange, if any, on which the Shares are principally listed or traded or (ii) the consent of the affected Participant, if such action would materially adversely affect the rights of such Participant under any outstanding Option, except to the extent any such alteration, amendment or revocation is made to cause the Plan to comply with applicable law, Stock Exchange rules and regulations or accounting or tax rules and regulations, or to impose any clawback provisions on any Options in accordance with Rule 11.

17.2 The Committee may establish sub-plans in order to comply with, take advantage of or otherwise in connection with any taxation, legal, regulatory or other rule, law, guidelines, regulations or other provision of or prevailing in any jurisdiction in which the Plan is or is intended to be operated.

18 Share Capital

The Company will maintain sufficient authorised and unissued Shares to enable it to satisfy the Options in full.

19 Termination

19.1.1 The Plan may be terminated at any time by ordinary resolution of the Company or by resolution of the Board and will in any event terminate on the tenth anniversary of the Adoption Date.

19.1.2 As from the date of any termination of the Plan under Rule 19.1 the Company will not grant any further Options but no such termination will affect or modify any subsisting rights or obligations of the Participants in respect of any Options already granted and notwithstanding such termination the Company will continue to act, administer and manage the Plan in accordance with its terms.

20 Notices

20.1 Notices to a Participant

Any notification or other communication to be given to a Participant in connection with the Plan will be deemed to have been duly given if sent either by electronic mail to the Participant's electronic mail address at his place of work, or by post in a pre-paid cover to the Participant's postal address last known to the Company or if sent to him at his place of work, and will be deemed to have been duly given on the date of dispatch or posting. The Group will have no liability whatsoever to a Participant in respect of any notification, document, payment or other communication so given, sent or made, nor will the Group be concerned to see that any Participant actually receives the same.

20.2 Notices from a Participant

Any notification or other communication to be given to the Company or any of its Subsidiaries in connection with the Plan will be delivered by hand or sent by electronic mail, fax or post to the registered office of the Company or the relevant Subsidiary or such other electronic mail or postal address as may from time to time be notified to Participants, but will not in any event be duly given unless it is actually received.

21 General

21.1 In the event of any dispute or disagreement as to the interpretation of the Plan, or as to any question or right arising from or related to the Plan, the decision of the Committee will be final and binding upon all persons.

21.2 Subject thereto the Committee's decision on any matter relating to the interpretation of the Plan and any other matter concerning the Plan will be final and binding.

21.3 The Company will bear the costs of setting up and administering the Plan.

21.4 Neither the Plan nor any action taken thereunder will be construed as giving any Eligible Person a right to be retained in the employment or service of the Group. No Eligible Person or Participant will be entitled to any compensation or damages whatsoever or howsoever described, by reason of any termination, withdrawal or alteration of rights or expectations under the Plan whether such compensation is claimed by way of damages for wrongful dismissal or other breach of contract or by way of compensation for loss of office or otherwise howsoever.

21.5 Any stamp duty chargeable on any instrument of the transfer entered into pursuant to each Option will be borne by the Company, or where relevant, any member of the Group in respect of Participants employed by it.

21.6 The Company will maintain all necessary books of account and records relating to the Plan.

21.7 The Committee will be entitled to authorise any person to execute on behalf of a Participant, at the request of the Participant, any document relating to the Plan, insofar as such document is required to be executed pursuant thereto.

21.8 The Participant will be responsible for obtaining any governmental or other official consent that may be required by any country or jurisdiction in order to permit the grant, vesting or exercise (as the case may be) of Options to or by him. The Company will not be responsible for any failure by the Participant to obtain any such consent or for any tax or other liability to which the Participant may become subject as a result of Options made hereunder.

21.9 The Plan will be governed by and construed and interpreted in accordance with Irish law and the Company and Participants agree to submit to the non-exclusive jurisdiction of the Courts of Ireland in relation to any claim, dispute or difference which may arise hereunder.

Exhibit 12.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Velichka Valcheva, certify that:

1. I have reviewed this Annual Report on Form 20-F of GH Research PLC;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's Board of Directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: March 5, 2026

By: /s/ Velichka Valcheva
Name: Velichka Valcheva
Title: Chief Executive Officer

Exhibit 12.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Julie Ryan, certify that:

1. I have reviewed this Annual Report on Form 20-F of GH Research PLC;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's Board of Directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: March 5, 2026

By: /s/ Julie Ryan
Name: Julie Ryan
Title: Vice President, Finance

Exhibit 13.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

The certification set forth below is being submitted in connection with GH Research PLC's Annual Report on Form 20-F for the year ended December 31, 2025 (the "Report") for the purpose of complying with Rule 13a-14(b) or Rule 15d-14(b) of the Securities Exchange Act of 1934 (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code.

I, Velichka Valcheva, the Chief Executive Officer of GH Research PLC, certify that:

1. the Report fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of GH Research PLC.

Date: March 5, 2026

By: /s/ Velichka Valcheva
Name: Velichka Valcheva
Title: Chief Executive Officer

Exhibit 13.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

The certification set forth below is being submitted in connection with GH Research PLC's Annual Report on Form 20-F for the year ended December 31, 2025 (the "Report") for the purpose of complying with Rule 13a-14(b) or Rule 15d-14(b) of the Securities Exchange Act of 1934 (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code.

I, Julie Ryan, the Vice President, Finance of GH Research PLC, certify that:

1. the Report fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of GH Research PLC.

Date: March 5, 2026

By: /s/ Julie Ryan
Name: Julie Ryan
Title: Vice President, Finance

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form F-3 (No. 333-285310) and on Form S-8 (Nos. 333-270422 and 333-285311) of GH Research PLC of our report dated March 5, 2026 relating to the financial statements, which appears in this Form 20-F.

/s/ PricewaterhouseCoopers
Dublin, Ireland
March 5, 2026